

# *The American Journal of* **DIGESTIVE DISEASES**

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**DEVOTED TO GASTRO-ENTEROLOGY AND NUTRITION**

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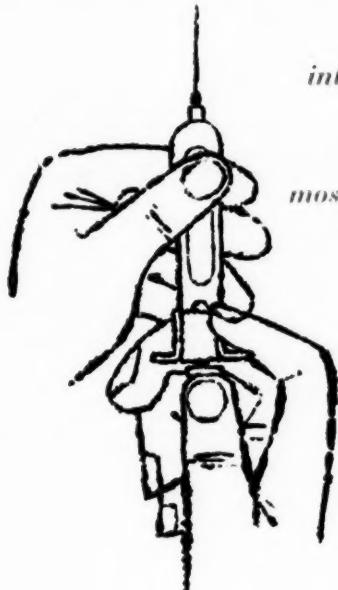
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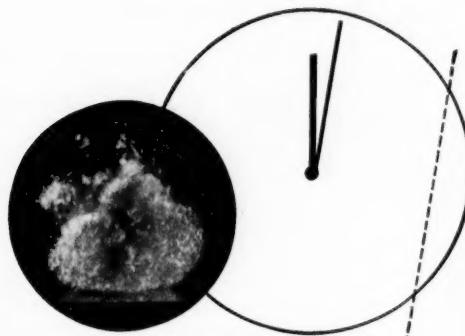
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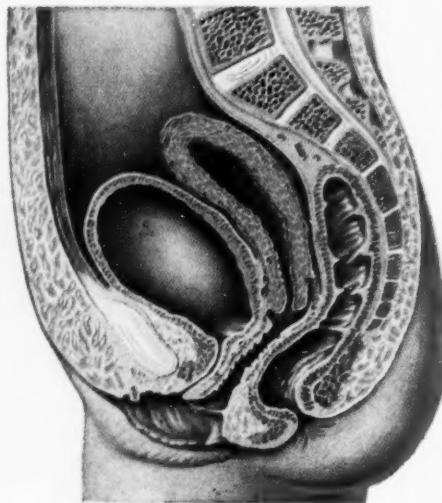
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# THE SUPERFICIAL CANCER OF THE GASTRIC MUCOSA

PROF. DR. G. E. KONJETZNY, Hamburg, Germany.

ACCORDING TO statistics our present methods of combat against gastric carcinoma do not express an essential progress in successful treatment. This is not to be wondered at, since our therapeutic efforts, even today, principally deal with developed gastric carcinoma, more or less advanced.

Therefore our hopes are concentrated on the possibility of a true early diagnosis in the sense of understanding the early stages of carcinoma growth, right from its very beginning. That is why the investigation of "gastric carcinoma in its beginning" was the central problem of nosologic research during the last ten years.

The result of fundamental research during the last ten years points to one firmly proven fact, that gastric carcinoma never develops in healthy gastric mucosa, but always in a morbidly prepared one (chronic ulcer, chronic gastritis with its sequels). A basic knowledge of the formation of gastric carcinoma is the essential

starting-point for the solution of this histogenetic problem.

This problem is so many-sided that it is impossible to do justice, in an objective way to every factor concerned, in such a short survey.

It has been satisfactorily proved and is now acknowledged that an ulcer carcinoma may occur and that hyperplastic chronic gastritis, with its pathologic and excessive regenerations, can produce cancer formation.

But it would be a completely insufficient understanding of the histogenetic process in the development of gastric carcinoma if one only considered the early stages of cancer formation, since from a mainly atrophic chronic gastritis, too, a gastric carcinoma may arise. An unquestionable proof of this has now been furnished.

With only a little space at my disposal, I can only give fragmentary hints of some facts which, to me, are significant.

The early stages of gastric carcinoma, here referred to, have been called "cancérisation en situ de la muqueuse gastrique" by Bertrand and as "oberflächlicher Schleimhautkrebs" by myself. These are very interesting phenomena, photographs of which are shown merely for information without considering their case histories. For in these cases we deal with results, which, up to the present, have been very little or not at all considered.

Macroscopically the "superficial mucosa carcinoma" appears in various varieties:

1. Very flat, irregularly defined, plaque-like, often widely extended erosions having a diameter of 8 cm or more, which can scarcely be seen by the naked eye, and even in section may escape the eye, if the preservation has not been expertly performed. Often a small chronic ulcer lies in the area of the serpiginous plaque erosions (Figs. 1, 2).



Fig. 1: Female, age 62, stomach complaints for nearly three years. Frequent nausea and vomiting, subacidity. Sharply bounded serpiginous erosions, nearly of the size of the palm of the hand, which were covered with plaqued grey-white pseudomembranes at the margin. The erosion, extending nearly to the pylorus, is more or less flat. In the center are small flat protuberances and pits which are also covered with yellow-white pseudomembranes (left: pylorus and duodenum).

Submitted Oct. 13, 1952.



Fig. 2: From the centre of the erosion (X15). Left: erosion with nests of glands; right: a small protuberance, with mucosa in process of transformation (x). On it, atrophic gastritis with irregular mucosal villi. Far right: a small protuberance as x. Inflammatory thickening of the mucosa. Irregular muscularis propria.



Fig. 3: x in Fig. 2 (X90). Mucosa replaced for the most part by tubular and solid irregular proliferations. Interstitial tissue very inflammatory. The covering epithelium is nearly all missing. At the bases of the protuberance remnants of pyloric glands. Muscularis mucosae inflammatory retracted.

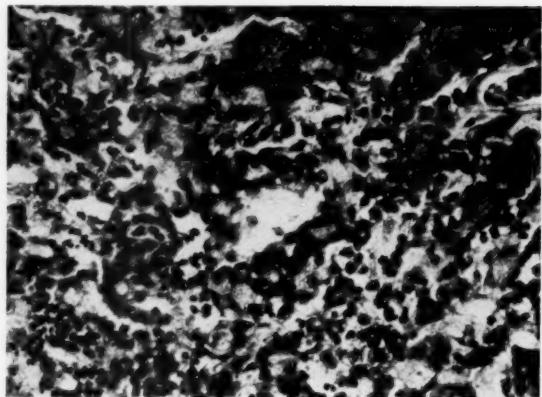


Fig. 4: Central part of fig. 3 (X450)—Irregular proliferation of polymorphic epithelium. Edematous stroma densely infiltrated by lymphocytes, leukocytes and plasma cells.



Fig. 5: Male, age 70. Stomach complaints for 17 years. Operation specimen cut along the greater curvature. Sharply bounded serpiginous erosion, half the size the palm of the hand, folds of mucosa breaking off at their margins. In its centre, at the lesser curvature, a flat small ulcer. Towards the pylorus and the posterior and anterior wall of the stomach mucosal protuberances, half the size of a pea, which project like islands from the flat erosion. Histological findings: almost identical with those in fig. 1 (left: pylorus and duodenum).

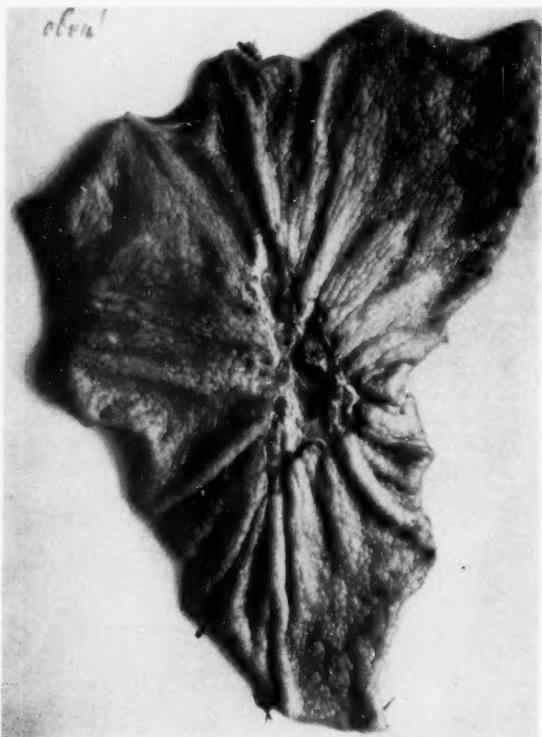


Fig. 6: Female, age 38. For two years stomach complaints, thought to be gastric ulcer. The last X-ray examination suggested cancer. Operation specimen, cut along, the great curvature: on the left, duodenum and pylorus. In the area of the angulus, overlapping the anterior and posterior walls of the stomach there is a triangular formation, at first thought to be an ulcer. This almost equilateral triangle lies with its narrow upper third on the anterior wall, and its broader lower two-thirds on the posterior wall. Margin serpiginous, flattened, in parts slightly raised. Base in the upper part flat, knobby, in the lower part roughened with pseudomembranes, especially in the marginal areas.



Fig. 7: Section through the upper narrow part of the triangle (fig. 6). The base of the triangular formation which at first sight appears to be an ulcer is not an ulcer, but a groove-shaped depression of the mucosa. The margins are formed by atrophic and partly atrophic-hyperplastic gastritis (X12).

2. Long, grooved, more plaque-like, bizarrely branched impressions and small cavities, of different sizes which, at first sight, look like an irregular flat ulcer. But these cavities and hollows lie only in the mucosal area (Fig. 6).

In the microscopic examination (low power) of these flat erosions one observes impressions and hollows, as well as the special chronic, subacute and acute inflammatory changes in this condition. An unorganized proliferation (still lying entirely in the mucosa) of contiguous and non-contiguous irregular tubular and solid strings and nests of polymorphic epithelium, sprouting from the covering epithelial proliferations through the muscularis mucosae into the submucosa cannot yet be recognized in the very early stages (Figs. 3, 7, 9, 10, 11, 15, 16).

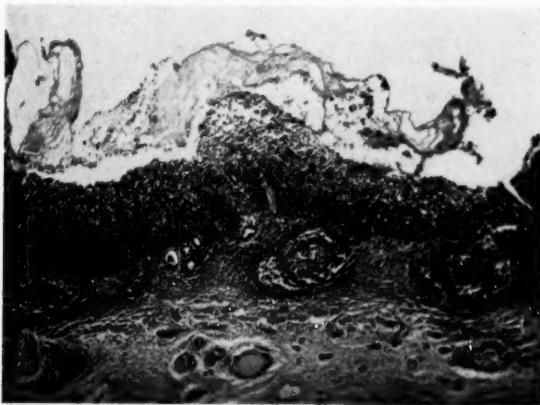


Fig. 8: Complete transformation of the mucosa [Fig. 7 (X60)]. At the base of the mucosa some remnants of glands. Elsewhere the mucosa is replaced by irregular tubular epithelium mostly solid proliferations of polymorphic cells. The interstitial tissue contains inflammatory cells placed close together. The surface is eroded with plaques, and covered with fibrinous exudate containing leucocytes. At the base of the mucosa lie three accumulations of lymphocytes. The muscularis mucosae is detached by an inflammatory edema, on the left broken up by heterotopic glands.

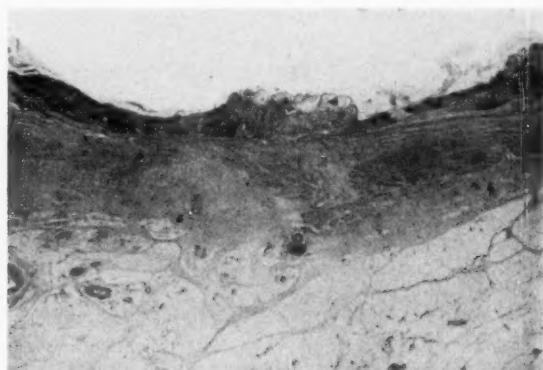


Fig. 9: Cross-section through the trough-shaped depression referred to in fig. 6 (X7). No ulcer. At the left the depression is covered by transformed flatly-eroded mucosa over which is a fibrinous exudate containing leucocytes (Histologic report similar to that of fig. 8). Towards the centre a mucosal protuberance is seen, followed by an erosion with small gland remnants and covered with exudate. The erosion extends to the muscularis mucosae. The margins of the depression show an atrophic gastritis. The muscularis propria is not interrupted. The submucosa is hypertrophic, the muscularis propria is partly destroyed and replaced by hypertrophic connective tissue.

Already in 1921 and in 1928 I had described and illustrated essentially the same states in atrophic gastric mucosa (7, 8). In 1938 I gave a detailed description (9), and supplemented it by later surveys (10, 11). In 1929 Bertrand (6) described conditions which were very similar to what I had already described.

The hypertrophic tissue extends to the mesogastrum. The proliferations just described were confined to the mucosa without showing any distinct signs of a destructive downgrowth or interruption of the muscularis mucosae. The nature of these pathological formations was doubtful. Thirty years ago I had already described them as forestages of canceration. But I did not call them cancer, if only the mucosa was involved. But in 1940 I could clearly prove that even this process was cancerous—an "oberflächlicher Schleimhautkrebs": by the following observation, the essential parts of which I briefly give here because of its fundamental importance.

#### CASE REPORT

Male, age 43. The anamnesis is very interesting. In 1922 dysentery. Since 1926 periodic stomach complaints which, in 1931, were variously treated as a suspected duodenal ulcer or heartburn. In 1939 further stomach complaints 1/2-1 hour after meals. Occasional vomiting. On 23rd Oct. 1939 admitted to internal medicine clinic. Good general condition, weight 81.3 kg, tongue coated, the highest result of the fractional gastric test-meal gave: total acidity 70; free HCl 34. Temperature 38.0°C, sore throat, throat-swab showed haemolytic streptococci, under treatment the pains improved, the temperature decreased to 37.8°C. Occult bleeding occurred.

X-ray examination: the lesser curvature is rigid in the area of the antrum, round the angulus a little depression in the contour of the lesser curvature, with flat ulceration in this area. The folds of the mucosa in the anterior and posterior walls of the stomach are thickened. Diagnosis: gastritis, with superficial ulceration at the angulus.

8th Dec. 1939: since early neoplasm could not be excluded, operation was performed. The findings were: perigastritis, pylorus slightly thickened. No pathological findings in the duodenum. Operation specimen of the stomach: At the angulus parallel with the lesser curvature, two flat ulcers covered with thick fibrinous membranes. In the area of these ulcers



Fig. 10: "Oberflächlicher Schleimhautkrebs" without infiltration of the muscularis mucosae, with pea-sized metastases in a regional lymph node. The section is along the lesser curvature towards the pylorus. The ulcer of the angulus is cut in half (in the photograph the relations are reversed, the left side being directed towards the cardia, and the right towards the antrum). On the left typical chronic ulcer; in the mesogastrum lymph nodes of the size of a pea.

The margin of the ulcer is flat, about 2 cm broad and consists of atrophic gastritis with the usual histologic appearance. Then follows a little thicker mucosa towards the pylorus, about 5-6 cm broad. Even under magnification it appears wholly transformed and eroded in plaques. Towards the pylorus there is mucosa showing the usual atrophic-hyperplastic gastritis.

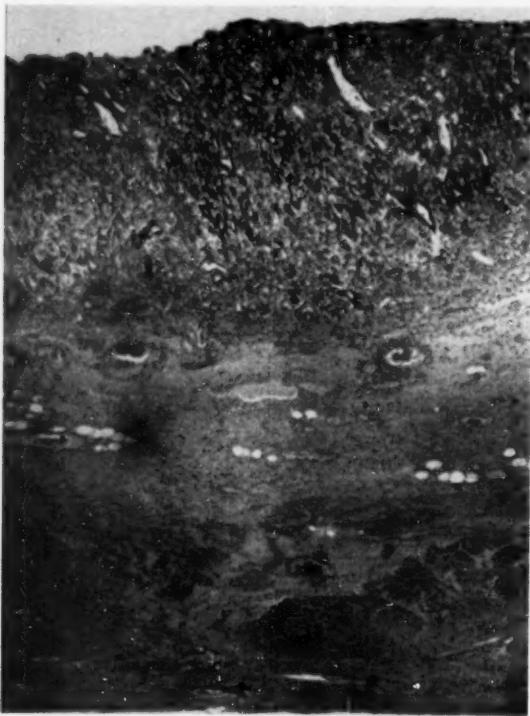


Fig. 11: x in fig. 10 (X29). Plaused erosion, complete transformation of mucosa. Total irregular, adenomatous proliferations covered with multilayered polymorphic epithelium. Irregular nests and tractions of polymorphic epithelial cells in the very cellular interstitial tissue. At the base of the mucosa some remnants of pyloric glands. There are leucocytes and inflammatory edema in the muscularis mucosae. Submucosa thickened with involved inflammatory cells. Perivascular infiltration of inflammatory cells. Dilated lymphatic vessels. There are inflammatory interstitial tissue and edema in the muscularis mucosae.

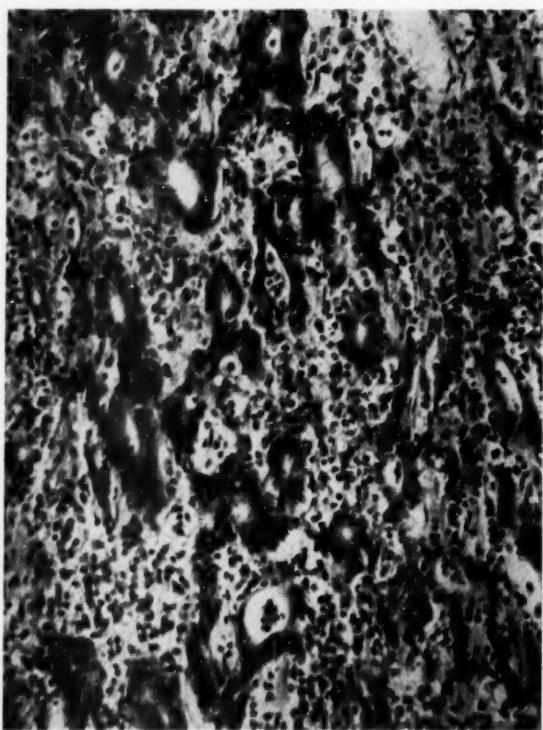


Fig. 12: Taken from the center of fig. 11 (X250). Tubular proliferations resembling adenocarcinoma with buds of irregular tractions and nests of polymorphic epithelial cells. Inflammatory interstitial tissue. A complete transformation of mucosa to a series of striae and wholly irregular proliferation of signet-ring cells.

small rigid thickenings of the stomach wall, which towards the pylorus become transformed into a flat erosion (with a diameter of 6-8 cm) and gradually vanish. Antral mucosa smooth, atrophic, fundal glands with thickened mucosa.

Dissection of the operation specimen in numerous large step-shaped slides of 8 cm and longer. I shall explain the microscopic findings with only four photographs (Figs. 10-13).

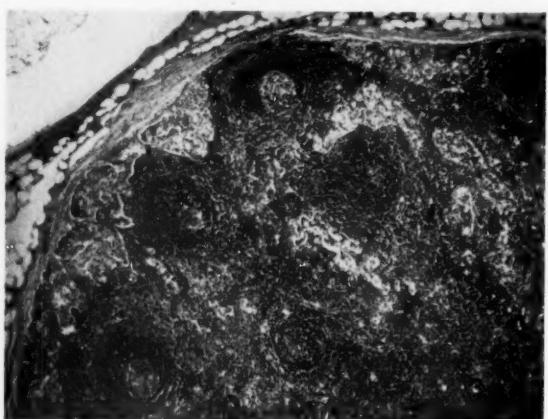


Fig. 13: The regional lymph node seen in fig. 10 (X50). In the marginal sinuses large cancer-cell nests; smaller ones, partly of tubular shape, also seen in other parts of the lymph node tissue.



Fig. 14: Male, age 73. No clear history. Nodular goiter, for which the patient had taken an iodine tablet daily for a long time. Clinical examination showed polypous and ulcerative transformations of the stomach walls at the antrum. 17th Sept. 1945 gastrectomy. Operation specimen cut along the greater curvature. On the left: pylorus and duodenum. Mucosa of stomach edematous, spotty, red. Along the lesser curvature, on the anterior wall and extending to the posterior wall, there is an irregularly demarcated erosion (a), size 4.5 cm. The base is partly covered by ragged grey-white pseudomembranes. A similar smaller erosion lies on the anterior wall towards the cardia (b). On the anterior wall there is also an oval erosion (c) on the posterior wall a plucked mucosal thickening (d) of a size of  $2\frac{1}{2}$  cm  $\times$   $3\frac{1}{2}$  cm.

The antral mucosa and neighboring part of fundal mucosa show an irregular relief with flat and warty formations which are clearly distinguished from the rest of the mucosa by their grey-white colour. These flat warty grey-white formations show an obvious similarity to a focal leucoplakia. At the lesser curvature there are several lymph nodes about the size of a pea.

In another case, besides two erosive cancerations, two plaque thickenings of the mucosa had also developed, rising above the level of the mucosa. The multicentric carcinoma origin, which in all other cases is clearly seen, in this case is especially obvious.

The observations on "superficial erosive mucosa carcinoma" of the stomach, of which we have only given some examples here, are not only of pathological-anatomical importance, but are also significant in general medicine because the condition is now clinically recognizable. In addition to the general clinical investigation, careful roentgenological examination of the gastric mucosa is of the highest importance. Although difficult,

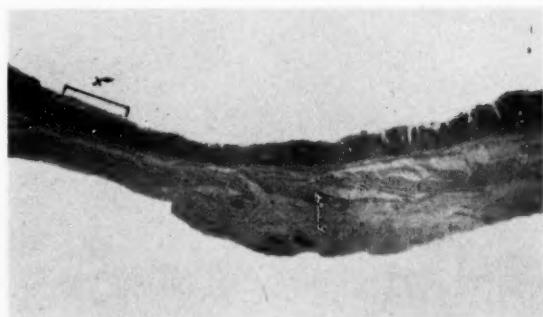


Fig. 15. Low power through the erosion in fig. 14a (X3). Complete transformation of the mucosa, replacement of the mucosa by irregular nests and rows of polymorphic epithelial cells and by adenomatous and papillary proliferations. The erosion b in fig. 14 is similar.

the roentgenological examinations can be successfully carried out, as is demonstrated by the results of my partner, the internist H. H. Berg and his collaborators Prévôt, Bücker and Schlotter. In this respect one may also look forward to diagnostic progress by gastroscopy.

Apart from early cancers of hyperplastic gastritis which nowadays can easily be detected, in my clinic, during the last years, we have made numerous gastrectomies in increasing numbers, even in cases of the so-called "superficial cancer of the mucosa."

Up to the present we had 48 cases. Without exception they were clinically diagnosed as suspected and as such were treated surgically.

The above are not chance findings but results based on conscious clinical consideration, and pathological-anatomical knowledge. That is a remarkable progress in the control of gastric carcinoma.

The roentgenological diagnoses of superficial cancer of the mucosa can, as mentioned above, only be an incidental finding at present. But a well-founded inci-

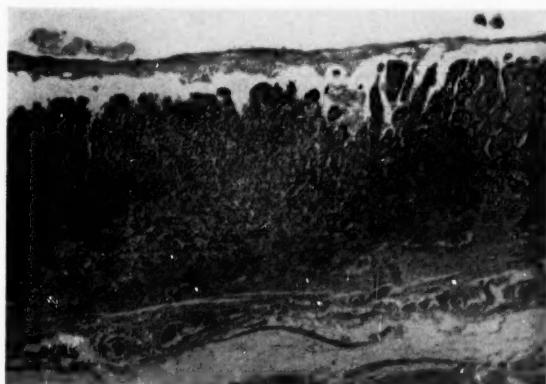


Fig. 16: x in fig. 15 (X40). The mucosa is formed by a proliferation of solid small nests and rows of polymorphic epithelial cells to the left, by an adenomatous and papillary proliferation to the right. Stroma rich in fibroblastic cells, infiltrated with leucocytes and lymphocytes. The surface of the mucosa is eroded, covered with fibrinous leucocytic exudate. Muscularis mucosae uninterrupted, inflammatorily infiltrated.

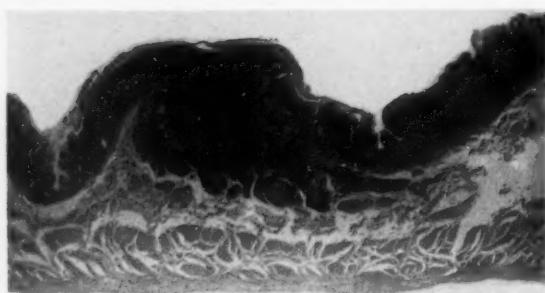


Fig. 17: Cross-section through the plaqued thickening of the mucosa (e). The eroded mucosa resembles that described in fig. 16. But the epithelial proliferation has extensively broken through the muscularis mucosa and invaded the submucosa. It is similar, but more pronounced to the plaque thickening of the mucosa d in fig. 14.

dental finding is essentially more important for the control of the gastric carcinoma than the diagnosis of an advanced gastric carcinoma. The efforts of the surgeon are of the same significance. When a well-founded clinical incidental finding is made, a great responsibility arises for the surgeon.

The decision for laparotomy is compulsory. But then the difficulties begin for the surgeon. For, under the usually rather obscure conditions of the biopsy he must decide what has to be done with the often scarcely discoverable stages: he has to decide whether to act or not. In short it is an important practical question, whether gastrectomy should be performed or not. One thing is as important as the other. In both cases the surgeon has the whole responsibility. He should not do any unnecessary operation, but he cannot abstain from a necessary one. Therefore he has to make a naked eye pathological-anatomical examination of the facts of the case and arrive at a provisional diagnosis.

But this task he can only fulfill if he is thoroughly acquainted with the pathological-anatomical conditions, which are decisive. For the right microscopic judgment one must have a great deal of experience together

with a mental picture of the pathological-anatomical transformations of the gastric walls.

Therefore it is quite clear, that the surgeon must do much more than carry out the operation in a careful, reliable, relevant way.

In recent years Albot and Toulet, Citerio, Collins and Gall, Prinz, Rössle, Schlotter have published further important contributions to the knowledge of superficial erosive cancer of the gastric mucosa.

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## THE PROBLEM OF ACUTE ABDOMINAL PAIN

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THE PROBLEM of acute abdominal pain is a perennially interesting topic. The subject never grows old. Nor can it be said that the problem has ever been fully analyzed, catalogued and filed away for immediate ready reference. Almost every year new diagnostic methods appear to add to the knowledge of the problem. These include new instruments of precision and countless chemical procedures to add to the understanding of some function or structure of the abdomen. Some of these tests prove to be of clinical value, many are of research interest principally, but all of them add to the complexity of the problem.

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Now abdominal pain is primarily a clinical problem and must be regarded as such. Any attempt to reduce it to a procedure subject to analysis by instruments of precision is doomed to failure, because the basic principles must be interpreted clinically rather than be measured chemically, optically or electrically.

Let us go back to first principles and enquire into the nature of pain. What is pain? And right here we encounter the first problem, because while everybody talks about pain, no one has so far come forth with even a satisfactory definition for it, much less any instrument of precision for measuring it, or of interpreting it even if such an instrument were developed. There is no accepted definition for pain. Pain has variously been described as a psychic phenomenon, as the cry of injured tissue, as a warning sign of danger, as

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an interference with the nutrition of tissue; while its antithesis, pleasure, is the enhancement of nutrition. It has been stated that any sensation which in small degrees may cause pleasure may if applied in larger measures cause pain.

Now there are two types of pain, and an appreciation of this difference is important in its understanding. There is (1) somatic or peripheral pain and (2) visceral or referred pain. Somatic pain originates in tissues having pain receptors and special sensory nerves for its transmission; while visceral pain originates in tissues that have no pain receptors or special sensory nerves for this function.

In the mechanism of somatic pain, a proper stimulus is required to initiate the pain impulse, such as mechanical, chemical, thermal, electrical, or toxic stimuli. The special pain receptors and sensory nerves are present to receive the stimuli, and the central apparatus for interpreting it must be intact. The mechanism proceeds as follows: (1) a proper stimulus is applied to a selected tissue, (2) which has special pain receptors and special pain nerves for the transmission of this impulse only, (3) the impulse is carried to the thalamus in the brain which identifies the pain and localizes it in the peripheral somatic area; (4) the ability to localize pain is a psychic phenomenon which has been acquired by experience.

Visceral pain on the other hand originates in organs that have no pain receptors or special sensory nerves for its transmission; hence ordinary pain stimuli applied to viscera cannot initiate pain. But viscera can and do cause pain as anyone knows from his boyhood experience of having eaten raw apples. The only demonstrable cause for visceral pain is ischemia or a state of impaired nutrition which occurs when an organ is forced to labor in ischemia or diminished blood supply.

The mechanism of visceral pain proceeds as follows: (1) a viscera is forced to labor in a condition of ischemia as a result of one of several reasons such as increased circulatory demands upon it, diminished blood flow as from the narrowing of the lumen of the supplying blood vessel such as occurs in arteriosclerosis, loss of normal elasticity, inflammations, etc.; (2) impulses thus initiated in the ischemic area are carried by the sympathetic nerves to their terminations in the spinal cord, (3) where a psychic transfer takes place, and (4) the impulses are received as coming from the sensory fibers of the same spinal level, (5) they are transmitted to the thalamus, (6) which refers them to the surface area supplied by these sensory nerves, (7) the pain is thus referred to the surface area which has the same embryonic segmental origin as the viscera which gave rise to the pain.

Visceral pain is thus referred not to the organ giving rise to it but to a surface area. For example, the heart develops in the cervical part of the embryo, although later it descends into the thorax; but it retains its innervation acquired in its early embryonic life. Later in the developed body, pain which originates in the heart is referred to the surface area which is supplied by sensory nerves which emerge from the same embryonic segment in which the heart developed originally. Accordingly cardiac pain is referred to the precordium, neck and arms.

So far, so good. But the problem does not end here. Several viscera may develop in the same embryonic segment, consequently they will refer their pain to the same segmental surface area. This phenomenon is apt to give rise to confusion in the interpretation of visceral pain. For example the stomach and kidneys develop in the same embryonic area and retain their developmental innervation into adult life from the celiac plexus and superior mesenteric ganglion, as do also the pancreas, liver, gall bladder, suprarenals, spleen and first half of the colon. In addition these organs receive fibers from the sensory-motor vagus nerve, which brings in impulses from all other parts of the body as well as the higher cerebral centers. (Ransom, Mettler).

In addition visceral pain is influenced by functions elsewhere in the body such as eating, sleeping, hunger, thirst, urinating, defecation, respiration, fever, anxiety, fatigue, disease processes, etc.

The size of a lesion producing pain is no index of the severity of the pain. Thus a pinpoint sized biliary gravel can cause as much pain as a large calculus.

Experience and memory teach a person to localize the pain. Visceral pain does tend to take on a definite pattern which is helpful clinically.

To add to the problem we have the factor of individual sensitiveness to pain. Not all individuals react the same to a given stimulus. The threshold for pain varies markedly with individuals and markedly with the same individual under varying conditions such as in hunger, thirst, fatigue, disease, mental concentration, economic pressure, etc.

Consider for example the patient who presents himself apologetically for epigastric distress and is found to have a cancer eating away his vitals; while on the other hand a neurotic gives an elongated history of his aches and pains, while examination shows him to be suffering with only a minor functional disturbance of the digestive tract. The inevitable conclusion is that the neurotic actually suffers more with his functional disturbance than the stoic does with his destructive disease.

Indeed if pain was the only symptom of disease it would prove very difficult at times to interpret it. But a disease process that gives rise to pain also affects the temperature of the body, the pulse, the blood pressure, blood count, functional appearance of the organ in the x-ray, blood chemistry and cytology, etc. It is by a consideration of all of these findings, that a clinical diagnosis is arrived at.

In addition to the disease processes within the abdomen that give rise to abdominal pain, there are numerous conditions outside of the abdomen which likewise give rise to abdominal pain. In fact the number of causes outside of the abdomen, far outnumber the causes found within the abdomen.

#### OUTLINE OF SOME COMMON CAUSES OF ABDOMINAL PAIN

##### A. Within the Abdomen

1. Gastric irritation.
2. Gastritis.
3. Gastric tumors.
4. Duodenitis.
5. Duodenal ulcer.
6. Enteritis.
7. Gall bladder inflammations.
8. Gall bladder functional up-

sets. 9. Gall bladder tumors. 10. Gall bladder concretions. 11. Hepatic tumors. 12. Hepatic inflammations. 13. Intestinal obstruction. 14. Pancreatic disease. 15. Colon irritation. 16. Colon inflammations. 17. Colon tumors. 18. Colon obstructions from within or without. 19. Appendicitis. 20. Adhesions. 21. Hernias. 22. Peritonitis. 23. Mesenteric accidents. 24. Soft tissue tumors of diverse origin. 25. Splenic diseases. 26. Other less common conditions.

#### B. Outside of the Abdomen

I. THE CENTRAL NERVOUS SYSTEM. 1. The emotional states. 2. Psychotic states. 3. Epilepsy. 4. Migraine. 5. Syphilis. 6. Brain tumors. 7. Inflammations of the brain and meninges. 8. Neuritis, etc.

II. THE HEAD. 1. Meniere's syndrome. 2. Otitis media. 3. Muscular imbalance of eye. 4. Nasal infections. 5. Oral infections, etc.

III. THE RESPIRATORY SYSTEM. 1. Upper respiratory infections. 2. Pleurisy. 3. Pneumonia. 4. Tuberculosis, etc.

IV. THE CARDIOVASCULAR SYSTEM. 1. Coronary disease. 2. Arteriosclerosis. 3. Congestive heart failure. 4. Endocarditis, etc.

V. THE GENITOURINARY SYSTEM. 1. Ureteral stricture. 2. Calculi. 3. Hydronephrosis. 4. Movable kidney. 5. Tumors. 6. Prostatic disease. 7. Nephritis, nephrosis, etc.

VI. THE PELVIS. 1. Pregnancy. 2. Tumors. 3. Mal-positions of the uterus. 4. Inflammations. 5. Hernias, etc.

VII. ANORECTAL DISEASE. 1. Hemorrhoids. 2. Polyps. 3. Tumors. 4. Cryptitis. 5. Proctitis. 6. Fistulas and sinuses. 7. Strictures, etc.

VIII. ACUTE INFECTIONS. 1. Scarlet fever. 2. Measles. 3. Small pox. 4. Influenza. 5. Tonsillitis. 6. Diphtheria. 7. Whooping Cough. 8. Typhoid. 9. Malaria, etc.

IX. TOXIC STATES. 1. Lead poisoning. 2. Arsenic poisoning. 3. Nicotine poisoning. 4. Alcohol poisoning. 5. Carbon disulphide poisoning. 6. Copper poisoning. 7. Aureomycin poisoning. 8. Sulfa drug poisoning, etc.

X. BLOOD DYSCRASIAS. 1. Pernicious anemia. 2. Myelogenous leukemia. 3. Lymphatic leukemia, etc.

XI. ENDOCRINE DISORDERS. 1. Hyperthyroidism. 2. Hypothyroidism. 3. Addison's disease. 4. Suprarenal deficiencies. 5. Gonad disease, etc.

XII. NUTRITIONAL DEFICIENCIES. 1. Pellagra. 2. Scurvy. 3. Vitamin B deficiency. 4. Acidosis, alkalosis, etc.

XIII. CONSTITUTIONAL DISEASES. 1. Allergies. 2. Arthritis. 3. Angioneurotic edema. 4. Amyloidosis. 5. Heat stroke, etc.

XIV. MISCELLANEOUS. 1. Diseases of the diaphragm. 2. Herpes intercostales. 3. Phrenectomy. 4. Other surgical procedures, etc.

#### MECHANISM OF REFERRED ABDOMINAL PAIN

There are five main pathways by which causes outside of the abdomen may refer their distress to the abdominal cavity.

##### 1. Common Innervation

The upper digestive tract including the stomach, small intestine, right side of the colon, gall bladder, liver, pancreas derive their innervation from the celiac and superior mesenteric plexuses and branches from the vagus nerves; however, these same nerves and plexuses also supply the kidneys and the suprarenals. The lower digestive tract including the right side of the colon, and rectum are supplied by the inferior mesenteric plexus and the pelvic nerves. However, these same nerves and plexuses also supply the urinary bladder, ureters, gonads and genitalia. Also there are connector fibers between the upper and lower digestive tracts.

Neuromuscular reflexes initiated elsewhere in the body including the higher cerebral centers may also be relayed to the digestive tract through the vagus and pelvic nerves.

##### 2. Metabolic Interrelationship

The digestive tract and other metabolic systems of the body are interrelated metabolically. Thus the digestive tract, kidneys and skin share in common their interest in water and salt excretion. The activity of one affects the activity of the others. Thus if any of these systems suddenly increases its excretion of water, it is immediately reflected in the reduced excretion of water in the other systems with a marked concentration of the solid portions of their excretions. Another instance of this metabolic interrelationship occurs whenever the stomach mobilizes the acid radicals of the body for purposes of digestion. This gastric activity is immediately paralleled by the alkaline tide of the urine.

The digestive tract is interrelated to other systems, as well as to several organs within the digestive tract, through various humoral substances which circulate in the blood stream. Thus the duodenal secretion within the circulation activates the pancreas. Various toxic products from all manner of fevers, intoxications and metabolic activities circulate in the blood stream to affect the activity of distant organs and viscera.

##### 3. Anatomic Relationship

Anatomically the digestive tract is surprisingly close to other systems. Only a thin peritoneal coat separates it from the genitourinary system and some of the pelvic organs. To some of these it is further attached by ligaments. Alterations of one system as by engorgement, inflammations, traction, tumor formation, etc. presses on or otherwise disturbs the circulation and nutrition of the other systems giving rise to symptoms.

##### 4. Endocrine Relationship

The endocrine systems elaborate endocrine products which circulate in the blood stream to influence the activity of distant viscera. Thus the endocrines elaborated in pregnancy depress the hydrochloric acid secretion of the stomach and give rise to nausea and

vomiting of pregnancy. The thyroid gland, the pituitary, the suprarenals and the gonads likewise elaborate secretions which influence the digestive apparatus.

### 5. The Circulatory Influence

The circulatory system influences the activity of the digestive apparatus in several ways.

Such degenerative processes of the vascular system as arteriosclerosis, coronary disease, thrombosis, etc., reduce the lumen of the blood source and so produce ischemia which is the primary cause for visceral pain.

Congestive heart failure produces portal congestion which sets up a whole train of mischief for the digestive tract.

Endocarditis gives rise to emboli which produce infarcts, regional ischemia and necrosis of viscera.

Now it is obvious from a consideration of these outlines that there are numerous causes for abdominal pain, and that many, if not most of them, originate outside the abdomen, and that the interpretation of abdominal pain at times presents difficulties. The more familiar types of abdominal pain are easily recognized, but some of the less common types present difficult diagnostic problems. Certainly there is no easy or royal road to the differential diagnosis of acute abdominal pain. It would be convenient indeed if there was a single or even a group of laboratory tests which would always give the answer to the problem of abdominal pain. Unfortunately there is no such easy convenient method, and abdominal pain still remains a clinical problem. To be sure in certain selected instances, the laboratory or x-ray will establish a diagnosis, such as the demonstration of a peptic ulcer, or a gall stone, or a tumor, or a positive Widal test, etc. But it is also true that in numerous instances the laboratory tests and x-rays are of doubtful value.

### A. ABDOMINAL PAIN ORIGINATING FROM CAUSES WITHIN THE ABDOMEN

(1) Gall stone colic. Sudden onset of agonizing pain beginning in the right hypochondrium and radiating to the right shoulder blade or epigastrium, associated with dyspnoea, coated tongue, elevation of temperature, tenderness in right hypochondrium, sometimes jaundice, nausea and vomiting.

(2) Duodenal ulcer. The ulcer syndrome is present consisting of "pain, food, comfort, pain." Heartburn at end of gastric cycle. Relief of pain by food, antacids, heat, vomiting, rest, antispasmodics. Finger point tenderness in epigastrium, hyperacidity, loss weight, sometimes vomiting.

(3) Appendicitis. Onset may be in right lower quadrant, epigastric or diffuse abdominal. Pain localizes in McBurney's area. Pain is colicky, later constant. Nausea and vomiting may occur. Coated tongue, constipation. Tenderness and rigidity in McBurney's area, fever, leucocytosis.

(4) Gall bladder dyspepsia. The syndrome of "fair, fat, forty and belching gas" usually present, belching, fulness after meals, flatulence, intolerance for certain foods. Distress diffuse in epigastrium.

(5) Salpingitis. Severe paroxysmal pain in one or both iliac fossae or in hypogastrium, sometimes diffuse,

may radiate to thigh. Vaginal discharge usually present. Specific microorganisms may be present in vaginal discharge. Tenderness is present in one or both tubal regions. Palpable mass may be present on bimanual examination. Fever, leucocytosis are present.

(6) Irritable Colon. Localized pain occurs under left hypochondrium, right hypochondrium, epigastrium, heartburn may be present, hyperacidity common. Abdominal consciousness, diffuse abdominal distress, headaches, coated tongue. Normal temperature and white blood count.

(7) Enteritis. Frequently sudden onset. Pain localizes about umbilicus. Pain tends to be colicky or crampy. Tenderness about umbilicus, coated tongue, fever, leucocytosis, tympanitis, borborygmi, diarrhea, prostration.

(8) Colitis. Tenderness along any or all of colon. Spastic tender colon especially in descending portion. Constipation, or diarrhea, or the two alternating. Diffuse colicky cramps. Prostration. Loss of weight, anemia, flatulence, liquid stools which may contain blood, pus or mucosa. Leucocytosis, low grade fever.

Gastric pain of any origin, whether on a functional, inflammatory or tumor basis is usually referred to a diffuse epigastric region. Pain arising on inflammatory basis is usually relieved by food. Tumor pain is usually aggravated by food taking.

Duodenal and pyloric pain is located in a very small area in the epigastrium or slightly to the left of it. Inflammatory conditions, including ulcer and diverticuli, are eased by food taking, but obstructive lesions are apt to be aggravated by ingestion of food.

Pain originating in the small intestine is apt to be located about the umbilicus. It is usually associated with tympanitis and diarrhea.

Pain of biliary dyspepsia, chronic cholecystitis and chronic hepatitis is frequently located diffusely in the epigastrium and sometimes in the right hypochondrium. Frequently the pain area of biliary disease occupies the same approximate position of gastric pain. There is usually also present fulness after meals, nausea, belching, sometimes vomiting, and intolerance for certain foods.

Biliary colic however usually has a different pain area than biliary dyspepsia. Biliary colic usually locates under the right costal margin in the approximate anatomic region of the gall bladder and radiates to the right scapula, epigastrium, left hypochondrium or down the right flank. It is a severe type of colicky pain usually requiring opiates for its control.

Colon pain will vary in its location depending upon the segment which gives rise to it. It may occur over any or all parts of the colon. It is usually associated with a change in the bowel habits. Sometimes constipation, sometimes diarrhea, sometimes the two alternating. Cramps and distention are also usually present. Sometimes the pain is not influenced by food taking, sometimes, however, there may be an associated hyperacidity in which case it is relieved by food taking and may even resemble the ulcer syndrome from which it must be differentiated.

Pancreatic pain is usually epigastric in its location, or it may correspond to the anatomic location of the

pancreas. The pain will vary in character depending on the lesion producing it. The pain may be dull, boring, constant, colicky, sometimes it may be aggravated by food taking.

Soft tissue tumors within the abdominal cavity as cysts, carcinomas, sarcomas, leiomyomas, Hodgkin's disease and numerous others arising from a great variety of tissues, hollow viscera, mesentery, blood vessels, fibrous tissue, smooth muscle fibers, etc., will cause pain, but the pain is not characteristic of the tumor; rather it takes on the characteristic of the organ with which it is identified.

Pain of intestinal obstruction is apt to be in the anatomic location in which it occurs. It is associated with muscular rigidity, tympanitis, muscle spasm, signs of shock, fever, tachycardia, leucocytosis, etc.

Pain of hernia origin both ventral and inguinal may be located in the lower abdomen as a dull constant ache aggravated by effort; or it may be referred to other parts of the abdomen and may even simulate peptic ulcer, gastric irritation syndrome, irritable colon or variants of these, as we have pointed out elsewhere.

#### B. PAIN ORIGINATING FROM CAUSES OUTSIDE OF THE ABDOMEN

##### 1. The Central Nervous System

The emotional states are the greatest single factor in the causation of abdominal pain. It has been stated by various writers that psychosomatic factors are responsible for thirty to forty percent of all the complaints that come to the internists' attention. Weiss believes that about one-third of all the patients presenting themselves have symptoms which are dependent on emotional factors. Sadler states that there are seven thousand babies born into the United States every twenty-four hours, and that twelve of these will reach adult life more or less neurotic. Ross states that minor examples of neurosis are found everywhere.

It is disconcerting to the young medical student to be told that the psychosomatic factors are responsible for more instances of abdominal pain than any other single factor, and in all probability more than all of the intraabdominal causes combined.

The differential diagnosis between functional disorders of the digestive tract due to psychosomatic factors and organic disease within the abdomen is made on (1) the history or neurotic background of the person as anxiety, apprehension, frustrations, etc.; (2) a family history of neurotic tendencies in other members of the family as a mother with a nervous headache; (3) the tremendous disproportion between the history of the patient as given and the physical evidences of disease; (4) exclusion of organic disease as incipient tuberculosis, hyperthyroidism, etc.; (5) a quantitative evaluation of the extent of the neurosis.

Functional disorders of the digestive tract may simulate organic disease to an annoying degree and seemingly present indications for laparotomies. One coal miner who came to our attention had had eight laparotomies at the time of his examination and stated that he still had the same abdominal pain that he had originally. He had psychoneurosis with referred abdominal pain.

Besides psychosomatic disorders, there are numerous other disorders of the central nervous system that give rise to abdominal symptoms.

Epilepsy often produces its prodromal phase in the abdomen, as nausea, vomiting, peristaltic unrest, regional abdominal consciousness; sometimes the principal attack may occur within the abdomen, by a form of paroxysmal abdominal pain, which is an epilepsy variant. This has been confirmed by electroencephalography studies and the therapeutic response to anticonvulsive drugs. (Moore)

The same may be said of migraine. Numerous writers have discussed the abdominal variant of migraine (King, Friedman, others). Like epilepsy it must be recognized from its general pattern, and response to therapeutic drugs as dihydroergotamine methanesulfonate (D. H. E. 45) which usually relieves an attack within a half hour.

Syphilis is a great mimic and may simulate organic abdominal disease. The tabetic crisis may cause severe abdominal cramps. Fortunately the diagnosis of this disease is reasonably simple by the serologic tests on the blood and spinal fluid.

Intracranial tumors may give rise to chronic dyspepsia syndrome, the peptic ulcer syndrome or acute paroxysmal attacks of pain, as we have pointed out elsewhere. A differential diagnosis is arrived at by a careful consideration of the symptomatology and neurologic and x-ray studies showing such anatomic alterations as destruction of the sella turcica, increase in the occipito-frontal diameter of the skull, widening of the sutures, the "beaten silver" appearance of the flat bones, the ventrilogram showing disturbances in the ventricles, neurologic findings as choked disc, ataxia, etc.

Various other disorders of the central nervous system produce abdominal symptomatology as intercostal neuralgia and neuritis which have been known to simulate acute appendicitis. The diagnosis is simplified by the appearance of the herpes.

##### 2. The Head

There are numerous conditions within the head other than diseases of the central nervous system that are capable of producing digestive disturbances. Among the common disorders are Meniere's syndrome, otitis media, muscular imbalances of the eye, nasal and oral infections. In 1929 Lebenthal demonstrated experimentally that reflexes occur from the eye to the stomach and from the stomach to the eye. Employing a stomach balloon connected with a water manometer, he made tracings to demonstrate the effect on gastric motility by astigmatic errors and muscular imbalances which he produced artificially by wearing cylinders and prisms. Errors of refraction and imbalances were definitely shown to exert a repressive effect on the motor functions of the stomach, while removal of such asthenic irritants was followed by a release of the inhibitory factors.

##### 3. Disease of the Respiratory System

Diseases of the respiratory system may cause abdominal symptoms. It is easy enough to see how a pleurisy affecting the diaphragm can by direct exten-

sion irritate or inflame the digestive organs; however, more remote thoracic processes can likewise cause abdominal symptomatology. Elsewhere we have pointed out that the onset of pulmonary tuberculosis may be gastrointestinal in character and that the patient may be treated for gastrointestinal disturbance for some time before the true nature of his disorder is uncovered. The mechanism of the referred symptomatology is believed to take place through the toxemia which occurs in the fever of the tuberculous process.

Likewise we have discussed the gastrointestinal manifestations of pneumonia; which likewise is regarded as taking place through the medium of the toxemia which is produced by the inflammatory process.

#### 4. Diseases of the Cardiovascular System

Cardiovascular disease produces digestive symptoms in a number of ways. First by producing ischemia and ischemia is the primary mechanism by which pain is produced in viscera. Arteriosclerosis and coronary disease narrow the lumen of blood vessels and reduce their elasticity and so produce ischemia and visceral pain. Indeed many of the cases of acute fatal indigestion described by our medical grandfathers were probably instances of coronary disease. Congestive heart failure causes passive congestion of the liver and congestion of the other abdominal viscera and so sets up a whole train of mischief in the digestive apparatus; endocarditis gives rise to emboli which cause narrowing of blood vessels, obstruction of blood vessels, infarcts of viscera with ischemia and sometimes necrosis, sometimes mesenteric thrombosis.

We have discussed elsewhere that cardiovascular disease may simulate "acute fatal indigestion," acute gall bladder disease, chronic gall bladder dyspepsia, ruptured abdominal viscera, renal colic, lead colic, malignancy. There is no pathognomonic sign for gastrointestinal symptoms of cardiovascular origin. The differential diagnosis is arrived at by a careful consideration of both systems aided by the electrocardiogram and blood studies.

#### 5. The Genitourinary System

The following renal disorders have been reported as being responsible for digestive symptomatology, namely stricture of the ureter, hydronephrosis, movable kidney, pyelitis, stone, tumor.

The genitourinary system produces digestive symptoms in a number of ways. First by close anatomic juxtaposition and ligamentous attachments, second by the chemical relationship, and thirdly by the common innervation, since both systems derive their innervation from the coeliac and superior mesenteric plexuses and branches of the vagus nerves. The chemical relationship is especially close. The activity of one system is closely interrelated with the other. An example, in diarrhea the urinary output is diminished. Numerous other instances may be cited.

Digestive symptoms of genitourinary origin are quite frequent and sooner or later every internist encounters instances of this interrelationship.

#### 6. Pelvic Disorders

Disorders of the pelvis produce digestive symptoms through (1) their anatomic relationship of contiguity,

ligamentous connections, peritoneal connections, (2) through their common innervation, since both systems receive fibers from the lower mesenteric ganglia and pelvic nerves, (3) through their metabolic relationship especially as a result of the endocrines elaborated by the gonads which circulate in the blood stream to set up reactions as the nausea and vomiting of pregnancy with the associated reduction of acid secretion of the stomach.

We have mentioned the following pelvic disorders as giving rise to reflex digestive symptoms: pregnancy, tumors, inflammations, malignancies, adhesions, malpositions, sinuses, fistulas, hypertrophies, foreign bodies, hernias.

Anatomically there is a very close relationship between the pelvic organs and the lower digestive tract. Inflammations, growths, malpositions, hypertrophies of either system press on the adjacent viscera setting up irritations and inflammatory reactions and reflex syndromes. Any abnormal growth in the pelvis will irritate the contiguous organs. Experience has shown that the correction of the pelvic disorder will often be followed by a cessation of the digestive symptoms.

#### 7. Anorectal Disease

Anorectal disease may refer its symptoms either locally or to other parts of the digestive tract including the upper abdomen. The symptoms may be referred to the epigastrum, upper abdomen, both hypochondria, or the entire abdomen. The symptoms may simulate a gastric irritation syndrome or an irritable colon syndrome and at times a peptic ulcer syndrome. The digestive symptoms are purely functional in character and usually subside when the offending anorectal lesion is corrected.

Elsewhere we have mentioned the following anorectal disorders as producing referred digestive symptoms: hemorrhoids, polyps, tumors, cryptitis, proctitis, fistulas, sinuses, strictures.

The mechanism of the production of referred digestive symptoms is regarded as taking place in the medium of the sympathetic and parasympathetic nerves. Irritation of the anorectal region gives rise to the irritable colon syndrome; this is followed by the gastric irritation syndrome and sometimes by the peptic ulcer syndrome.

#### 8. The Acute Infections

Practically all of the acute infections produce digestive symptoms. Typhoid fever is the outstanding example, but then typhoid is primarily a disease of the small intestine. However, all the other known infections as influenza, scarlet fever, etc. produce at times nausea, vomiting, tympanitis, cramps, loss of appetite, distention, borborygmi, abdominal pain, etc.

In many of the infections the abdominal pain bears little if any physiologic relationship to the infection which produces it, since the abdomen has little direct relationship to the tissues which are involved and which give rise to the abdominal distress. The symptoms result from the toxemia which is elaborated by the fever process and which causes the viscera to labor under strain and impaired nutrition.

Elsewhere we have discussed the toxemia which is elaborated in a fever process, stating that generally (1) a non specific toxin resulting from the general fever process, and (2) a specific toxin elaborated by the specific microorganism causing the infection which is antigenic in character and often forms the basis for the specific serologic tests of the disease.

#### 9. The Toxic States

Toxic states can produce abdominal symptoms, as poisoning from lead, arsenic, mercury, nicotine, alcohol, copper, aureomycin, sulfonamides, carbon disulphide, and others.

Aureomycin is well known for its ability to produce side reactions as pharyngitis, gastritis, enterocolitis, resulting in a loss of appetite, nausea, vomiting, diarrhea, abdominal pain, cramps, distension, etc. Sulfonamide toxemia likewise produces a gastroenteritis with marked resultant symptoms referable to these organs. It has been shown both experimentally and clinically that the toxic manifestations are both local and central in origin. The central origin is easily demonstrated by inducing vomiting by the intravenous injection of the sulfonamide drugs, while the local origin is easily demonstrated also by the intravenous injection of sulfapyridine when the vomitus is found to contain a greater concentration of the sulfonamide drug than the blood stream.

If taken in large doses the heavy metals can produce a hemorrhagic gastroenteritis which may terminate fatally. In lead poisoning the liver and intestines are among the primary depots where the heavy metal is deposited. Abdominal colic is an early manifestation of lead poisoning.

#### 10. The Blood Dyscrasias

The blood dyscrasias are well known for their tendency to produce digestive symptoms. Pernicious anemia frequently has its onset with digestive symptoms in about thirty percent of the cases. The tongue becomes smooth, red and free of papillae. The gastric mucosa becomes atrophied and inflamed, the liver tends to enlarge. Burning and soreness of the tongue appear, likewise epigastric distress and fulness, gas distress, diarrhea, achlorhydria.

The leukemias, both the myelogenous and the lymphatic cause splenic enlargement and to a lesser extent some hepatic enlargement. Enlargement of the spleen causes a heavy sensation in the left hypochondrium and sometimes a bulging. Hemorrhages may occur from the digestive tract.

#### 11. The Endocrine System

The endocrine organs may produce gastrointestinal symptoms. Indeed hyperthyroidism, according to Robertson, Wohl and Robertson, may at times have a distinctive gastrointestinal onset, which may even suggest an acute "surgical" abdomen. In two cases that they observed, the abdominal signs and symptoms mimicked acute appendicitis. One of these patients was operated on and revealed a normal appendix. Other writers have reported indigestion, pain in the abdomen, and bearing down pains in hyperthyroidism.

The mechanism of the abdominal symptoms is be-

lieved to result from the disturbed metabolism affecting the vegetative nervous system.

Addisons disease is well known for its tendency to produce anorexia, nausea and vomiting and pigmentation of the mucous membranes, also gaseous distention and occasional episodes of intense diarrhea.

#### 12. The Nutritional Deficiencies

The nutritional deficiencies have long been known to produce digestive disturbances. Scurvy caused by vitamin C deficiency has long been known as the plague of soldiers, sailors and prisoners. Indeed prior to the present century, scurvy has defeated as many armies and navies as armor and bullets have, and on numerous occasions has changed the course of history. For centuries scurvy has been known as the pestilence of the seas and its insidious onset with loss of appetite, loss of strength, swollen gums, loss of teeth, dyspepsias and gastrointestinal hemorrhages. Fortunately except in the very far advanced stages scurvy is a reversible disease and the administration of even a small amount of citrus fruit juice or vitamin C will correct the process.

Pellagra is caused by a deficiency of vitamin B complex and is likewise insidious in its onset. In the past it has been quite prevalent among our southern population because of their dietary habits. Pellagra is characterized by certain skin disorders and disturbances of the central nervous system as well as digestive disturbances. The mucosa membrane of the digestive tract show swelling, ulceration, reddening in any or all parts. The liver may contain abnormal amounts of fat. Glossitis may occur, also stomatitis, gastritis and enteritis.

Minor vitamin B deficiencies are common today even among the so called better element of society, especially in a generation that has learned to eat and enjoy white bread, candies, concentrated foods, from which the bran, minerals and vitamins have been removed and discarded as though they were some noxious substance. Many of our "best" hotels and families still scorn to serve whole wheat products as something quite vulgar. Their refined food with its white bread and concentrated foods is still capable of producing minor vitamin B deficiencies with their resultant loss of appetite, asthenia, constipation, flatulence, gaseous distention, abdominal consciousness, fulness after meals, abdominal distress, etc.

Acidosis and alkalosis produce toxic changes in the body which interfere with the normal chemical activity of the digestive tract. Sometimes they even set up a vicious cycle. Thus in peptic ulcer with obstruction treated with alkalies, there may result persistent vomiting with a loss of the acid radicals of the body and a resultant alkalosis, and the alkalosis in turn causes vomiting to continue the vicious cycle.

#### 13. The Constitutional Diseases

For the want of a better classification, we have grouped here such disorders as allergies, angioneurotic edema, amyloidosis, arthritis, and heat stroke, all of which produce a toxic effect on the digestive tract giving rise to symptoms.

Allergies take on a great variety of forms and simulate gastritis, enteritis, colitis, appendicitis, cholecys-

titis, etc. Diagnosis is arrived at by the history of allergic reactions in the body, the skin tests, elimination diets, desensitization tests and antihistamine therapeutic tests.

Arthritis and rheumatic fever may have their onset with episodes of acute gastroenteritis which may at times simulate appendicitis. Some writers caution delay in opening the abdomen of patients with rheumatism or arthritis for supposed appendicitis until a therapeutic trial has been given with anti-rheumatic therapy. The digestive symptoms result from two sources, (1) the toxemia which occurs from the disease process, and (2) the impaired circulation.

Heat stroke fortunately is rare in the temperate areas of our country, but it does occur at times sufficient to merit our attention, especially after a prolonged hot spell and in congested metropolitan areas. Elsewhere we have reported a study of one hundred fifty-eight cases of heat stroke observed in the Cook County Hospital of Chicago during the month of July 1916 following a particularly hot spell.

Practically all of the patients manifested some digestive symptoms as polydipsia, anorexia, nausea, vomiting, diarrhea, epigastric distress as well as the constitutional symptoms of headache, hyperpyrexia, dizziness, malaise, tachycardia, stupor, etc. The mortality in our series was 44 percent.

Amyloid liver occurs in long wasting diseases as tuberculosis, syphilis, chronic arthritis, malignancies. The liver becomes enlarged, extends into the abdomen, presses on the contiguous organs and interferes with their blood supply and nutrition and so gives rise to symptoms. Also the disease process gives rise to a toxin which serves as an irritant to the digestive tract.

#### 14. Miscellaneous

Diseases of the diaphragm such as hiatus hernia give rise to symptoms in some instances. Herpes intercostales may simulate abdominal disease especially in the stage before the appearance of the herpes. Phrenectomy and other surgical procedures may disturb the normal anatomic relationships of the digestive tract and give rise to a whole train of symptoms.

These are some of the common causes of abdominal pain. It is evident from even a superficial inspection of the list that the majority of instances of abdominal pain are caused by factors which exist outside of the abdomen. The abdomen has aptly been called the barometer of the body. It tells of trouble but does not locate it. The psychosomatic factors are the largest single etiologic factor being responsible for about a third of all the cases of abdominal pain encountered in private practice by the internist. However, in a spirit of fairness it must be stated that there are some die-hard followers of the organic theory who still insist that if we but look hard enough we will find some anatomic alteration to account for the existing symptomatology.

Be that as it may, the fact remains that there is no easy or royal road to the differential diagnosis of acute abdominal pain. It is necessary to have a reasonable knowledge of clinical medicine in its broad aspects. The principal danger lies in having too limited an out-

look. Likewise it is very unwise to attempt to make a diagnosis based largely on laboratory or x-ray data. X-rays, blood counts and a whole army of chemical blood tests are helpful and will in an occasional case establish a diagnosis, but in themselves they are inadequate. There is no substitute for the clinical study of the patient and an analysis of his symptoms.

Epigastric pain even when relieved by food taking can be caused by lots of things besides peptic ulcer. Pain in the right lower quadrant likewise can be caused by lots of things other than the appendix.

We record here a single clinical case of acute abdominal pain to illustrate the inherent difficulties of making a diagnosis at times. In this case the x-rays and laboratory data were "negative." The diagnosis was ultimately made by an analysis of the symptoms.

#### CASE REPORT

##### ACUTE ABDOMINAL PAIN WITH AUTOPSY

J. M., a farmer of 44 years, was admitted to the General Rose Memorial Hospital of Denver on October 19, 1950 because of severe abdominal pain in the hypogastrium three days in duration. The pain radiated upward to the umbilicus. The pain had come on suddenly without warning. It was a dull constant boring pain occupying the position of a distended urinary bladder, if the bladder had been distended which it was not. The pain radiated upward to the umbilicus. It did not radiate down to the thighs, nor down to the genitals, nor to the back. The pain was so severe on admission that it required the immediate administration of sedatives. The patient, a man of a high degree of intelligence, was emphatic in localizing the pain in the hypogastrium radiating up to the umbilicus and in no other direction. The pain was aggravated by food taking and it eased up at the end of the gastric cycle. Otherwise he had some headache and constipation and no other complaint of importance.

Physical examination showed a 44-year-old white male weighing 220 pounds, 6 feet in height, of florid complexion which was slightly cyanotic. His temperature was 100, his pulse was 104, his respiration was 18, his blood pressure was 200/120. He was in evident distress. He was a large person with an obese abdomen. The eyes, mouth and throat were within normal limits. The chest was of normal configuration. The lungs were within normal limits. The heart was of the transverse type. There were no murmurs. The aortic second sound was accentuated. The pulse was rapid. The abdomen was completely relaxed. It was quite adipose and difficult to examine, nevertheless there was no muscle spasm. The pain was indicated in the hypogastrium. The liver and spleen were not palpable. The prostate was normal, the rectal examination showed some small hemorrhoids.

He was voiding normally. The urine was within normal limits. The blood count showed a red count of 6,000,000; a white count of 17,200 with 65 percent polys, 32 percent lymphs and the remainder transitional. A flat film of the abdomen was taken and showed normal gas pattern and no evidence of intestinal obstruction or tumor formation or stones. A proctoscopic examination showed the small hemorrhoids, but otherwise a normal colon with normal mucosal pattern. The reflexes were equal and slightly exaggerated. There was no evidence of spinal cord or brain damage. A Wassermann was not made. It was not considered necessary at the time. J. M. had a family of healthy children.

A diagnosis could not be made on admission. He was treated symptomatically. He was given sedatives, antibiotics, intravenous medication, vitamins.

Fortunately we had seen him four years previously and had access to his history at that time. In 1946 he had come to us complaining of epigastric pain, fullness after meals, belching, bloating. He had admitted to excessive use of alcohol. The examination in 1946 showed a gall bladder which filled and emptied well, the gastrointestinal tract had shown marked irritability. The blood pressure had been 150/86. The electrocardiogram had been normal. The diagnosis in 1946 had been (1) Chronic Alcoholic Gastritis, (2) Overweight 42 pounds.

Since 1946 something had happened to his blood pressure and now it was 200/120.

In attempting to make a diagnosis, we listed the positive findings. These were (1) pain in the hypogastrum radiating up toward the umbilicus three days in duration, (2) the pain was aggravated by food taking, (3) hypertension 200/120 which had developed in the past four years, (4) history of alcoholism, (5) leucocytosis of 17,200 with 65 percent polys.

The pain, we considered, was the key to his case. Anatomically it was in the region of a distended urinary bladder, but the bladder was not distended and functioning normally. The prostate was normal, the lower colon seemed to be within normal limits, the small hemorrhoids were in themselves insufficient to cause the acute symptomatology presented by the patient. There was no evidence of spinal cord or brain injury. The pain did not conform to common patterns of diseases of the gall bladder, stomach, small or large intestines, and the flat plate ruled out intestinal obstruction.

There remained the symptom of hypogastric pain which was made worse by eating or on digestive effort. We have seen instances of mesenteric arteriosclerosis in which this occurred. Additional factors pointing to a circulatory problem were the hypertension, arteriosclerosis and history of alcoholism. We considered an arteriosclerosis of the mesenteric blood vessels as the underlying cause and basis of his pain.

The patient continued to get worse clinically, with an aggravation of his pain, restlessness and intolerance of all foods. The symptomatic treatment was continued.

On October 21, 1950 at 9 A. M. he had a sudden attack of excruciating pain in the same region. He went into shock quickly. His pulse became very rapid and thready, the cyanosis increased markedly, he vomited bile, he perspired freely and he was clammy. His abdomen became stiff and board-like in hardness. He was immediately placed in an oxygen tent. At this time we were fairly well satisfied that he had a ruptured viscus, but which one? If it was a digestive organ or some tumor such as a pedunculated cyst, we would open him immediately as an emergency. However, if it was a circulatory accident, then opening him would only hasten his end. We decided that he had had a circulatory accident and elected to leave him in the oxygen tent.

At this time we made a clinical diagnosis of Ruptured Dissecting Abdominal Aneurism.

The man continued to get worse. He became moribund. Extravasated blood appeared in his flanks. He died on October 26, 1950.

Postmortem examination showed the presence of: (1) Ruptured dissecting aneurism of the abdominal aorta, (2) general arteriosclerosis, (3) massive hemorrhage into left retroperitoneal tissues, (4) passive hyperemia of abdominal viscera, (5) arterial hypertension, (6) hypertrophy of the heart (680 grams) (7) patchy fibrosis of the myocardium. Cause of death: Massive retroperitoneal hemorrhage.

In 1951, Herschowitz and Bagg reported their study of sixteen cases of aneurism of the abdominal aorta. They stated that 22 percent coexisted with thoracic aneurism, the others were independent occurrences. In thoracic aneurism, syphilis was the etiologic factor in 84 percent of the cases; whereas in abdominal aneurism syphilis was responsible for only 25 percent of the cases, while arteriosclerosis was responsible in 69 percent and infected emboli was responsible in 6 percent.

#### SUMMARY

1. Abdominal pain is primarily a clinical problem. In spite of all the instruments of precision and chemical tests, it remains primarily a clinical problem.

2. All visceral pain is referred pain, and is referred not to the organ giving rise to it, but to the surface area supplied by sensory nerves which arise in the

same spinal segmental level at which the viscera developed embryonically.

3. The threshold for pain varies markedly with different individuals and with the same individual under varying conditions such as hunger, thirst, fatigue, anxiety, economic pressure, etc.

4. The causes for abdominal pain originate both within and outside the abdomen.

5. The extra-abdominal causes far outnumber the intra-abdominal causes.

6. The common causes for abdominal pain which originate within the abdomen are the diverse disturbances of the stomach, small and large intestine, appendix, gall bladder, liver, spleen, pancreas and mesentery.

7. The common causes for abdominal pain originating outside of the abdomen are: disturbances of the central nervous system of the head, the respiratory system, the cardiovascular system, the genitourinary system, the pelvis, the anorectal region, acute infections, toxic states, blood dyscrasias, endocrine system, nutritional deficiencies, constitutional disease, miscellaneous disorders.

8. There are five main pathways by which causes outside of the abdomen transmit their symptoms to the abdomen: These are (a) the common innervation with some other system, (b) the metabolic interrelationship, (c) the anatomic relationship, (d) the endocrine relationship, (e) the circulatory relationship.

9. The more familiar types of abdominal pain are easily recognized for the clinical entities that they indicate: but some of the less common types present serious difficult diagnostic problems.

10. Epigastric pain even when relieved by food taking can be caused by numerous causative agents other than peptic ulcer, such as psychoneurosis, hyperacidity, mucous colitis, irritable colon, anorectal disease, etc.

11. Likewise pain in the right lower quadrant can be caused by numerous agents other than appendicitis, such as pneumonia, rheumatic fever, hyperthyroidism, intercostal neuralgia, right sided genitourinary disorders, right sided pelvic disease, adhesions, etc.

12. The differential diagnosis of abdominal pain is made by a careful clinical study of the patient aided by the laboratory and x-ray studies.

13. The aid of the laboratory tests is recognized as being very useful, but its role must not be over emphasized.

14. There is no easy or royal road to the differential diagnosis of acute abdominal pain.

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## INVESTIGATION OF ENTERIC INFECTIONS IN THE CARIBBEAN AREA\*

### I. A SURVEY OF INTESTINAL PARASITISM IN LOMBARDIA, MICHOACAN, MEXICO

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THE PARASITOLOGICAL survey reported in this study was conducted in the town of Lombardia, in the region known as "The Tepalcatepec Basin," in the state of Michoacan, Mexico. As this region has been designated as an experimental epidemiological center by the Rural Cooperative Medical Services\*\*, and the Inter-American Cooperative Public Health Service\*\*\*, the purpose of the study was to contribute to the existing knowledge of the incidence of intestinal parasitism in this area. This survey was instituted as a result of discussions between the Field Party of the Institute of Inter-American Affairs of Mexico, representatives of the Rural Health Service of Mexico, and the Tropical Research Foundation of Chicago. The months of February and March, 1952, were selected as the most favorable time for carrying out this study.

The town of Lombardia was chosen as the site for the study because the sanitary conditions, health habits, and mode of living of the people were considered as representative of the region. Located 350 miles south-

west of Mexico City, Lombardia has a climate that is tropical, an elevation of 2460 feet, and no rainfall during the months of February and March. The town is composed of approximately 3,584 people, the majority of whom are farmers. Sanitary conditions are extremely poor. There are very few outhouses and the majority of the people pass their excretory wastes in open areas. Those outhouses in use are generally constructed over small streams that flow through the town. These streams, in turn, provide the water that is utilized for the usual household chores, and at times, for drinking purposes. The main source of drinking water is an aqueduct from whence it is piped directly into the town. This, however, does not ensure satisfactory drinking water, because, prior to reaching Lombardia, the aqueduct passes through several ranches where water is contaminated with human and animal wastes.

#### METHOD

Fecal specimens were obtained through the cooperation of the local medical personnel. Paper ice cream cups containing 10 percent formalin as a preservative were used to collect the specimens. The subjects were instructed to place a specified amount of a freshly passed fecal specimen in the cup and completely emulsify the specimen in the preservative fluid with the tongue depressor blade provided with each cup. This procedure was emphasized in order to ensure the adequate preservation of all organisms. Two specimens were submitted on separate occasions from approximately one-half of the individuals under study. One specimen was obtained from each of the remainder of the group.

Direct microscopic examinations, using saline and Lugol's iodine solution (1), were made on the preserved fecal material. In conjunction with the direct microscopic examination, approximately one hundred samples were studied using the salt flotation method of Willis (2).

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\*This is the first of a series of papers relating the findings of a survey party sent out by the Tropical Research Foundation and by the Lasdon Foundation to study enteric diseases in the Caribbean area, under the directorship of Dr. Oscar Felsenfeld.

\*\*The Rural Cooperative Medical Services, an agency of the Ministry of Public Health and Welfare of Mexico, operates in this region with the cooperation of the Tepalcatepec Commission, an official organization for the development of the area.

\*\*\*The Inter-American Cooperative Public Health Service is an entity within the Ministry of Public Health and Welfare of Mexico, formed by bilateral international agreement between Mexico and the United States through the Institute of Inter-American Affairs.

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TABLE I  
Incidence of Parasitism in Relation to Age and Sex

Age in Years	1-10	11-20	21-40	41-80	Unknown	Total
Sex: male	77	27	26	11	19	160
female	65	26	54	13	20	178
total	142	53	80	24	39	338
<b>PROTOZOA</b>						
Endamoeba histolytica	%	%	%	%	%	%
male	41 53.2	15 55.6	12 46.2	6 54.5	4 21.1	78 48.8
female	30 46.1	17 65.4	23 42.6	5 38.5	2 10.0	77 43.3
total	71 50.0	32 60.4	35 43.8	11 45.8	6 15.4	155 45.9
Endamoeba coli						
male	55 71.4	15 55.6	9 34.6	7 63.6	10 52.6	96 60.0
female	33 50.8	16 61.5	31 57.4	7 53.8	10 50.0	97 54.5
total	88 62.0	31 58.5	40 50.0	14 58.3	20 51.3	193 57.1
Endolimax nana						
male	39 50.6	8 29.6	9 34.6	3 27.3	7 36.8	66 41.3
female	29 44.6	16 61.5	25 46.3	8 61.5	5 25.0	83 46.6
total	68 47.9	24 45.3	34 42.5	11 45.8	12 30.8	149 44.1
Iodamoeba buetschlii						
male	17 22.1	6 22.2	3 11.5	4 36.4	1 5.3	31 19.4
female	7 10.8	9 34.6	10 18.5	1 7.7	3 15.0	30 16.9
total	24 16.9	15 28.3	13 16.3	5 20.8	4 10.3	61 18.0
Giardia lamblia						
male	7 9.1	4 14.8	1 3.8	0	2 10.5	14 8.8
female	4 6.2	1 3.8	2 3.7	0	0 0	7 3.9
total	11 7.7	5 9.4	3 3.8	0 0	2 5.1	21 6.2
Chilomastix mesnili						
male	1 1.3	0	0	0	0	1 0.6
female	0 0	0	0	0	0	0 0
total	1 0.7	0 0	0 0	0 0	0 0	1 0.3
Trichomonas hominis						
male	0 0	0	0	0	0	0 0
female	1 1.5	0	1 1.9	0	0	2 1.1
total	1 0.7	0 0	1 1.3	0 0	0 0	2 0.6
<b>HELMINTHS</b>						
Ascaris lumbricoides						
male	30 39.0	7 38.6	2 7.7	1 9.1	3 15.8	43 26.9
female	22 33.8	9 34.6	12 22.2	1 7.7	5 25.0	49 27.5
total	52 36.6	16 30.2	14 17.5	2 8.3	8 20.6	92 27.2
Hymenolepis nana						
male	8 10.4	5 18.5	0	0	0 0	13 8.1
female	8 12.3	3 11.5	0	0	1 5.0	12 6.7
total	16 11.3	8 15.1	0 0	0 0	1 2.6	25 7.4
Taenia sp.						
male	1 1.3	1 3.7	0	0	0	2 1.2
female	0 0	1 3.8	0 0	0	0	1 0.6
total	1 0.7	2 3.7	0 0	0 0	0 0	3 0.9
Necator americanus						
male	1 1.3	2 7.4	0	0 0	0 0	3 1.9
female	1 1.5	1 3.8	0	1 7.7	1 5.0	4 2.2
total	2 1.4	3 5.7	0 0	1 4.2	1 2.6	7 2.1
Trichuris trichiura						
male	3 3.9	0 0	0	0	0	3 1.9
female	1 1.5	1 3.8	0	0	0	2 1.1
total	4 2.8	1 1.9	0 0	0 0	0 0	5 1.5
Strongyloides stercoralis						
male	2 2.6	0 0	0	0	1 5.3	3 1.9
female	1 1.5	1 3.8	0	0	1 5.0	3 3.3
total	3 2.1	1 1.9	0 0	0 0	2 5.1	6 1.8
<b>NEGATIVE</b>						
male	8 10.4	4 14.8	8 30.8	3 27.3	6 31.6	29 18.1
female	12 18.5	3 11.5	12 22.2	1 7.7	7 35.0	35 19.7
total	20 14.1	7 13.2	20 25.0	4 16.7	13 33.3	64 18.9

## DISCUSSION AND CONCLUSIONS

The results of the survey are summarized in Table 1. The data, obtained from a study of 338 individuals, are divided into specific groups to illustrate the distribution of age and sex within this population sample. Concomitant with these data, the percentage of each specific parasitic infection is recorded for the respective sexes within the various age groups, together with the percentage of positive infection for the entire population. The results obtained using the Willis flotation method were compared to those obtained for the entire study using the direct microscopic examination procedure, and the differences were not found to be significant. One can attribute this to the large number of parasites that were noted when an individual stool was positive for a specific infection.

The data indicate that the majority of the individuals studied were less than twenty years of age. On the whole, the sex distribution among the younger age groups (1-20 yrs.) was quite uniform. In the next older age group, there was a predominance of females. Since the average life span of individuals in this area is approximately forty years and because at the time the specimens were collected the adult males were usually working, these factors may account, in part, for the unequal sex distribution in the third age group and for the majority of individuals being classified in the younger age groups.

The incidence of parasitism in this population was found to be very high. Approximately eight out of every ten individuals, or 81.1 percent of those studied, harbored at least one type of parasite. Multiple infections were quite common with 62 and 20 percent of the positive cases having from 1 to 3, and from 4 to 6 different parasites, respectively. The most common type of parasitic infection was protozoal, which was found to be distributed evenly throughout the population, independent of sex and age. Hegner et al. (3) determined the incidence of *E. histolytica* in Morelia, Michoacan, Mexico, and their finding of 23 percent was lower than our figure of 45.9 percent obtained in the Lombardia survey. As the survey by Hegner was conducted in the capital city of Michoacan, a more urban community with considerably superior sanitary

conditions, the incidence of the infection in this township is understandably less.

Among the helminthic infections, the only parasites of importance in Lombardia appear to be *Ascaris lumbricoides* and *Hymenolepis nana*, whose incidences were 27.2 and 7.4 percent, respectively. Although we are limited by the total number of individuals studied (338), there appears to be a greater number of helminthic infections among the lower age groups as contrasted to the protozoal infections which were more evenly distributed throughout the population.

## ACKNOWLEDGEMENT

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## SUMMARY

A parasitological survey was carried out in the town of Lombardia, Michoacan, Mexico. The data show that the overall incidence of intestinal parasitism among the 338 individuals studied is 81.1 per cent. The only parasites of importance in Lombardia appear to be *Endamoeba histolytica*, *Ascaris lumbricoides* and *Hymenolepis nana*, whose incidences were 45.9, 27.2 and 7.4 per cent, respectively. The incidence of these and other parasites are listed with a breakdown of their distribution among the population sample.

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## THE TREATMENT OF MIGRAINE, GOUT AND HEBERDEN'S NODES (A factor common to these conditions)

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TO DATE the widespread literature relative to the causative factors, underlying pathology and treatment of Migraine, Gout and Heberden's Nodes, bears out the lack of specific treatment for the same.

For many years we have noticed a factor common to these conditions—a factor that may have a bearing on the precipitation and/or exacerbation of attacks and in the treatment of the same. This common factor must be stressed if progress of these conditions may possibly be halted, attacks prevented and, in Gout and

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Heberden's Nodes, improvement brought about before permanent deformity occurs. The common factor noticed is as follows:

A greater than normal sensitiveness to the higher or readily soluble carbohydrate foods than generally found. This sensitiveness is particularly noticeable in the Migraine cases and more marked if the higher or readily soluble carbohydrate foods are taken during the latter part of the day, as this tends to build up the blood sugar level in the individual to the height where precipitation of an attack occurs in the early morning,

even though this level is well within the normal range of blood sugars.

On the other hand, many Migraine sufferers can avert and avoid attacks if sufficient water is imbibed within a relatively short time, to flush the blood sugar and keep it below the attack level.

In the experimental years we were able, in Migraine cases, to precipitate attacks by giving glucose or other sugars per rectum as retention enemas in order to side-track gastric upsets. We also enabled these people to more rapidly terminate the attacks by flushing the bowel, at 2 to 4 hour intervals, with plain warm water per rectum and allowing a quart of water to be retained, at the same time giving them from 2 to 4 glasses of water every hour orally. Administration of greater or lesser amounts of protein and fatty foods had no effect on the precipitation or progress of the attacks.

The carbohydrate foods designated must be kept within the individual's tolerance (which is determined through trial and error) at a level low enough to avoid headaches. The longer the interval between attacks the less apt the patient is to precipitate headaches by carbohydrate indiscretion. Gradually, over a long period many Migraine patients noticeably increase their tolerance to these carbohydrate foods, although this increased tolerance almost always remains below the normal level and may retrogress under sufficient indiscretion. Another noticeable factor that frequently tends to bring on attacks is excessive sweating without water replacement, which concentrates the blood sugar to headache precipitating levels.

In cases of Gout and Heberden's Nodes, we could frequently:

1. Precipitate exacerbations or acute attacks of the same by increasing the higher or readily soluble carbohydrate foods while maintaining normal or less than normal protein intake.
2. Clear up the exacerbations or acute attacks by reducing the higher or readily soluble carbohydrate foods and by increasing the water intake.

Even sharply increasing all types of protein intake, the source of uric acid and urates, to above normal levels simultaneously with this sharp decrease of the carbohydrates, in conjunction with the increase of water intake, did not halt or adversely affect the course of improvement. In other words, there seems to be a definite sugar/nitrogen ratio that is important in preventing the precipitation of attacks of Gout and Heberden's Nodes (urates and uric acid). If the sugar/nitrogen ratio is lowered to within the individual's tolerance it will tend to avoid exacerbations or flare-ups of attacks. If this ratio is raised beyond the individual's tolerance, attacks can be precipitated, at times, within 48 hours. Here again excessive sweating, without water replacement beyond the individual's thirst, may also precipitate the attacks.

In setting up a dietary regime the following foods are prohibited:

1. Nuts and legumes.
2. Gravies and fatty meats, such as goose, pork and pork products (except lean ham or Canadian bacon).

3. Mayonnaise and salad oils.
4. Fruit and vegetable juices, milk beverages, beer and soft drinks (except those sweetened with saccharin or sucaryl).
5. Cereals (except in limited amounts as potato substitutes).
6. Jellies and preserves.
7. Dried fruits.
8. Fruit canned in syrup.
9. Rich cheeses.

The following foods are permitted in limited quantities within the patient's tolerance:

1. Fried foods (occasionally).
2. Cream, butter or margarine (as a thin spread on bread but not in cooking); and other shortenings.
3. Chocolate (Sweetened with saccharin or sucaryl).
4. Plain cookies or cakes, pies, pastries or puddings (all in very limited quantities sweetened with sucaryl or saccharin and without dried fruits or nuts).
5. Custards, ice cream or other frozen desserts if sweetened with sugar. (Greater amounts are tolerable if sweetened with sucaryl or saccharin and with a minimum of milk).
6. Cream soups.
7. Cheese (restricted because of lactose content).
8. Potato or substitutes such as noodles, macaroni, rice etc.
9. Bread, rolls or hot breads.
10. 20% vegetables.
11. 15% vegetables.
12. 10% vegetables.
13. Fresh or "water-pack" fruit.
14. Liver (normally would be unlimited but is restricted here because of glycogen content).

The following foods are permitted in unlimited quantities:

1. 5% vegetables.
2. Lean meats (including lean preserved meats if preservatives are removed by parboiling).
3. Fowl (except goose).
4. Fish and shell fish (canned sea foods may be used in unlimited amounts if oil and similar packing materials are removed by washing in hot water).
5. Eggs.
6. Broths or meat stock soups (either plain or containing allowed meats or vegetables. Excess fat should be removed).

#### SUMMARY

1. A factor common to cases of Migraine, Gout and Heberden's Nodes is a greater than normal sensitivity to the higher or readily soluble carbohydrate foods.
2. In Migraine cases there is solely a carbohydrate sensitivity not related to protein or other foods.
3. In cases of Gout and Heberden's Nodes there is a definite sugar/nitrogen relationship, the sugar factor being the important one.
4. The dietary regime for treatment of the above is described herein. 218 E. University Parkway.

## BIOLOGICAL BASIS OF AN ALIMENTARY REGIME PREVENTING INTESTINAL FERMENTATION AND INTOXICATION

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RESEARCH UPON a special regime to prevent intestinal fermentation was brought about by the conditions of nutrition which were imposed on us in Paris during the last world war.

Complaints of intestinal fermentation became much more frequent and its manifestations more apparent as time went on. Looking for the reason in the mode of nutrition of that time, we noticed that the outstanding feature of it was not so much the quantitative scarcity of food, as its qualitative monotony; we lived chiefly on rutabagas, or potatoes, or kidney-beans, or macaroni, and such carbohydrate foods. Meat and butter were very limited, fresh salads rare, fruits and milk completely absent, milk having been reserved for children and old people over 70.

As our human cells are not identical in structure with those of any ordinary foodstuffs, the body needs a variety of foods in order to be able to synthesize its own specific substances. The intestinal epithelial cells, which are in charge of this task, need not only all necessary elements ("Bausteine" of Abderhalden) for this synthesis, but they need them well mixed together at the same time. If there is anything missing, the food passes by, without being assimilated (London and Dobrovolskaia 1909, Dobrovolskaia 1911 and 1913).

Striking evidence of the need for a mixture of foods is given by the ability of the intestinal villi to produce not only the movements of a sucking pump, but also lateral whipping movements which mix the chylous masses in their neighborhood.

This fundamental physiological requirement for a variety of food was not fulfilled during war time, and the first result of it was insufficient assimilation. The people were always hungry, they tried to eat as much as possible of the only food which was available, but in spite of that they were not satisfied, and continued to get thinner and thinner.

The incomplete utilization of ingested food was shown by the enormously increased quantity of excrement, which was often of a semiliquid character. This liquefaction was of especially frequent occurrence among the people who were eating large amounts of soup and were absorbing with it not only more liquid, but also much sodium chloride.

The non-assimilated part of the already hydrolyzed food represented a good nutritive medium for bacteria, multiplication of which was finally the fundamental cause of the observed intestinal fermentation.

Inadequate nourishment and intoxication from abnormal intestinal products were accompanied by a series of quite characteristic clinical manifestations: loss of weight, aerophagy, abdominal swelling, easy fatigability, vertigo and disequilibrium in walking, less efficient work, and so on. In addition, many people were annoyed by diuresis, frequent and urgent micturition, and urinary incontinence.

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Using mice as laboratory animals, we reproduced all these clinical manifestations experimentally by means of certain products of intermediary metabolism (pyruvic and lactic acids) and a hypertonic solution of sodium chloride (Dobrevolskaia-Zavadskaia et al.). Quite characteristic lesions were found microscopically in the organs of these animals; their clinical corollaries were confirmed by means of the determination of B.B.S. (bisulphite binding substances) in the urine of the patients. We described this condition as a pathological entity under the name of "pyruvism," corresponding to the accumulation of pyruvic acid in the organism. The sodium chloride, toxic by itself, aggravated the action of pyruvic acid, since the  $Na^+$ -ion plays a very important part in the spasmodic manifestations of this metabolite. Softened feces and urinary disturbances are a frequent occurrence in pyruvism aggravated by a high salt intake. A continuously unbalanced diet with a predominance of carbohydrates is one of the causes of "pyruvism" and intestinal fermentation. On the other hand, overeating, a too abundant nutrition in general, also produces intestinal fermentation, and may be responsible for various pathological conditions.

In a recent book on the origin of diseases, Daubresse (1951) bases his "unitary theory" of general pathogenesis on the importance of the alimentary factor. His patients with eczema were mostly overnourished, fleshy persons; their food intake in 24 hours sometimes attained four to five thousand calories. On being submitted to a drastic restrictive diet which reduced their weight to what it had been at the age of 25 years, they could be cured in a few weeks.

Fletcher and his followers (1903-1930) also aimed at the restriction of the quantity of ingested food through careful and prolonged mastication. Many postulates of "Fletcherism" are quite reasonable, but they should be supplemented by new data concerning the qualitative composition of the diet.

There is no doubt that many people are accustomed to eating much more than they need. They do so because eating is a pleasure, or because they think it is necessary in order to stay healthy; but mostly it is because they feel hungry. A variety of foods, however, is essential for good assimilation, insufficiency of which is the main cause of a continuous feeling of hunger. A simple calculation of ingested calories as proteins, fats and carbohydrates, such as is generally accepted, does not suffice, because assimilation depends not only on quantitative proportions, but also on the quality of various foods, their appetizing character (psychologic stomach juice of Pavloff), and perhaps on some unknown factors which are contributed by a variety of natural foods.

Practically speaking, rational nutrition may be reduced to one hot dish at each meal, 200-250 ml. of milk, 50-70 gr. of bread, 10-15 gr. fats (butter, or olive oil, or peanut butter,—even better, a little of each), 20-25 gr. of meat, salad, green vegetables and various fruits

as desired. For one person, occupied in sedentary or light physical work, the hot dish may consist of a mixture of vegetables cooked in a small quantity of water, well covered to keep in the steam.

The importance of vitamins in normal nutrition is well known. We recommend eating green vegetables and fruits together with cooked food. Such a procedure assures the admixture of vitamins with every particle of ingested food, contributes to better assimilation and, by enveloping roughage with softened cooked food, renders it innocuous even for a very delicate digestive mucosa, such as exists when there is a catarrhal or even an ulcerous condition. A middle-aged woman who had suffered many years from such a condition reported, after a few months of our regime, that she had forgotten ever having had an ulcer. This woman, however, presented an increased quantity of pyruvic acid in her urine, and we added to her diet one tablet of Benerva forte (vitamin B<sub>1</sub>) after each meal. Vitamin B<sub>1</sub> is scarce in our ordinary foods, which need to be supplemented by a synthetic product in the case of pyruvism. The favorable effect of such a combined treatment was confirmed in another analogous case where there had been a profuse intestinal hemorrhage.

Progressive inhibition of intestinal fermentation, the result of improved assimilation, certainly played its part in these two cases. The reality of improved assimilation is made evident by the possibility of considerably reducing the amount of ingested food (to as little as half of the former quantity) without causing hunger or loss of ordinary working capacity.

Another sign of decreased fermentation is the aspect of the feces. They should be well formed, not soft, and should fall to the bottom without adherence and without clouding the water. Fulfillment of this last condition shows that all water-soluble items of the ingested food were well absorbed by the intestinal wall. Having had no available nutritive medium, bacteria did not multiply and did not produce putrefaction accompanied by gases, and thus such feces are not offensive to the nose.

It takes time to elaborate an individual regime, but once adopted, it may be maintained as long as all excess is avoided. Each occurrence of foul-smelling feces shows that something was eaten in disproportion to the other ingredients of the diet, or that something was lacking, or too much was eaten. Of course, all these considerations hold as long as there is no infection and the food does not contain any deteriorated items, being freshly prepared or at least brought to the boiling point immediately before eating it.

It is often considered that the absorption of the digested food depends on peristalsis: increased peristalsis leads to diarrhea, and decreased to constipation. In connection with this, we have an observation which indicates that the condition of the feces may also depend on assimilation. A woman ate a plate of beet soup, one evening, with a little bread and practically nothing else. She experienced distension in the night; next day her stool was soft and foul smelling. The following evening she once more ate beet soup, but also a small piece of meat and a handful of cooked and raw vegetables. Next day the feces were well-formed and without any foul odor. This shows that the supplemented meat and vegetables furnished the amino-acids, vi-

tamins, and probably some other unknown items which were lacking in the first case and which are necessary for thorough assimilation.

This statement was confirmed by many other people and an additional observation was obtained: sometimes only a relatively small part of the feces are liquid, the neighboring portions being well-formed. We interpret such an occurrence as a sign of an insufficient mixture of the ingested food in the digestive tube itself. This appears logical, since the main, if not the only movement exhibited by this tube is a peristaltic one, i.e. the pushing ahead of the nutritive materials in the same order as they were taken in. In the stomach some hard masses may be retained by the pylorus, but even the stomach does not display any lateral mixing movements. That is why we agree with the requirement of *Kouchakoff*, 1937, that the ingested food must be well mixed in the mouth by thorough mastication.

With such a varied and well-mixed diet, practically no foodstuffs are prohibited (except, of course, for some special pathological cases). Even such foods as cabbage, kidney beans, and peas may be taken without difficulty and contribute to the nutritive value of the meal, if eaten in quite small quantities together with other things. On the contrary, the most digestible foods—meat, fats, rice, macaroni, sweets—may not be fully utilized by the organism and may even poison it if taken alone and in great quantity. Overeating of fats causes stones in the liver, arteriosclerosis, angiomatous transformation of the intestinal mucosa (*Dobrovolskaia-Zavadskaya and Monsikoff* 1951) and perhaps sometimes its cancerization. The excessive intake of proteins may contribute to arterial hypertension, gouty conditions and arthritic changes. The predominance of carbohydrates, such as rice, macaroni, and sweets, which cause an accumulation in the organism of pyruvic acid, may be surmised in people with a tendency to hypotension, or in persons suffering from aerophagy, cramps, muscular pains, easy fatigability, disturbed walking and respiration, arrhythmia and so on. By greatly reducing the use of rice, macaroni, and sweets and adding vitamin B<sub>1</sub>, we obtained quite satisfactory results in many cases of pyruvism. The prevention of intestinal fermentation doubtless also played a salutary part.

The intervention of a latent pyruvism in hypertension explains why *Kempner's* regime produces in some patients quite unexpected complications: being based on the consumption of much rice, it increases the accumulation of pyruvic acid in the organism, enhances pathological manifestations facilitated by this accumulation, and is therefore impracticable.

Nevertheless, we do not forbid a small piece of chocolate at the end of the meal or a few sweets and fruits.

Concerning the rate of quantitative reduction of food, we have already mentioned some numerical data.

However, the restriction of food should be individually determined by each subject according to his energy requirements, his life and his activities. If the proposed regime is correctly prepared, the total amount of food may be easily reduced to two-thirds and later to half of the accustomed amount. The correctness of the reduction may be judged by the following criteria: 1) the feeling of hunger should not return before 6-7 hours after a meal; 2) the efficiency

of work should be completely preserved and even improved, and 3) a thorough inspection of the feces should not reveal any sign of continued intestinal fermentation.

The control of weight is also a very important test: it has to be maintained in persons of normal weight; it may increase in thin ones, and should diminish in cases of obesity. In connection with the last requirement, we have had an instructive observation. A rather short but heavy man, already operated on for stones in the ductus choledochus, and complaining of aerophagy, tenderness of the liver and many disagreeable abdominal sensations, wanted to get thinner. We found in his urine an increased quantity of pyruvic acid and treated him by means of a series of intravenous and intramuscular cocarboxylase ("Roche") injections, and also our diet. He returned a few weeks later quite satisfied about his pains but disappointed about his weight; it had increased in spite of the reduced amount of food. This reduction being surely insufficient, his improved assimilation overshadowed it.

We fully realize that the main obstacle that may prevent the popularity of our diet is a very deep-seated fear of not eating enough: by eating more than they need, people destroy their health. It has been observed that mice and rats fed a restricted diet live longer (Moreschi, 1909; McCay, 1952).

#### CONCLUSIONS

The fundamental physiological requirement for preventing intestinal fermentation is thorough assimilation of ingested food. Thorough assimilation cannot be secured without a complete variety of foodstuffs, cooked as well as raw, and eaten at the same time in small quantities.

When thorough assimilation of digested food takes place, there remains no nutritive medium for bacteria, and intestinal fermentation does not develop.

Success in preventing intestinal fermentation may be judged by the appearance of the feces: they should be well formed and odorless and should fall to the bottom without clouding the water and without showing adhesiveness.

The observation of feces is a very important factor in determining the efficiency of digestive function: each relapse to foul-smelling excrement signifies a faulty diet.

The proposed regime not only preserves health and nervous equilibrium but reduces food expenses.

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## ABSTRACTS ON NUTRITION

PAGE, I. H. and CORCORAN, A. C.: *Dietary treatment of hypertension*. Jour. of Clin. Nutr., 1, 1, Sept.-Oct. 1952, 7-16.

A minority of patients with established essential hypertension respond favorably to diets containing about 0.2 gm. sodium in each day's intake. Protein intake may be sustained by sodium-poor milk powder, or sacrificed, as in the rice diet. Usually a 6 weeks' trial of the method will establish its usefulness or

otherwise. Cation-exchange resins are not as yet adequate substitutes for rigid sodium restriction. The use of hexamethonium in conjunction with the low sodium diet is definitely a good combination.

ALBANESE, A. A.: *The effects of amino acid deficiencies in man*. Jour. of Clin. Nutr., 1, 1, Sept.-Oct. 1952, 44-52.

Albanese presents data which support the view that in protein-depleted states a diet poor in one essential

amino acid may be more deleterious than one poor in proteins. Certain amino acid deficiencies in man can be identified by changes in amino acid levels in the urine or blood. The development of chromatographic procedures has simplified this approach to the study of nutritional states. Possibly we shall soon know more about the aberrations of amino acid metabolism in various diseases, and be able to develop a rational system of specific amino acid therapy.

BRUCH, H.: *Psychological aspects of reducing.* Psychosomatic Med., XIV, 5, Sept.-Oct. 1952, 337-346.

The familiar theme of obesity resulting from emotional maladjustment and consequent overeating is again emphasized, but Bruch brings out a less familiar aspect of the subject by stating, "To the emotionally disturbed obese person, weight reduction has an irrational meaning, namely, that of fulfilling exaggerated day-dreams of success and achievement. For such people reducing cannot be considered a harmless procedure. If rigidly enforced it may precipitate serious mental disturbance, even psychosis."

KWASHIORKOR II.: *Clinical picture, pathology and differential diagnosis.* Brit. Med. J., Oct. 11, 1952, 798-801.

Edema is a constant feature of all advanced cases involving the feet, the face and genitalia. Ascites is rare. A fair amount of subcutaneous fat may be retained. The "crazy-pavement dermatosis" which appears first in the inguinal region and spreads to all pressure areas is perhaps pathognomonic, even though it is transient. The hair, normally black, becomes flaxen or reddish. Mental apathy is profound. At Mulago, there is seldom any gross hepatic enlargement. There is a palpable anemia which responds, but slowly, to treatment by high protein diet. Notable pathological lesions include the disappearance of zymogen granules from the pancreatic acini and the accumulation of fat in the periphery of the hepatic lobule.

WILLIAMS, R. J.: *Alcohol as a nutritional problem.* J. Clin. Nutrition, 1, 1, Sept.-Oct. 1952, 32-36.

From his study of rats, Williams found that those rats which were on a marginal diet (deficient) were more prone to choose alcohol than water as a beverage. Already, the clinical application is being made and it has been found that many alcoholics, when given heavy vitamin supplements, especially when vitamin B<sub>12</sub> was included, improved so that they "could drink or leave it alone." Williams's fascinating and underlying theory is that some individuals possess a distinctive enzyme pattern with certain requirements that are seldom if ever filled by their diets. Thus he regards alcoholism as an example of a genotrophic disease, i.e. one which arises because the genetic pattern of the individual calls for an augmented supply of a particular nutrient or nutrients, which is not supplied by the food consumed. There may exist a multitude of such diseases.

NELSON, A. M.: *Blood lipid correction in arteriosclerosis and its hypotensive effect.* Northwest Med., 51, 10, Oct. 1952, 860-866.

Thirty-three arteriosclerotic patients, 22 of whom had hypertension, were treated by the use of a high protein, low fat, low cholesterol diet and by lipotropic agents orally, and B vitamins with high pyridoxine

content, parenterally. It was sought to lower blood cholesterol levels and raise the phospholipid-cholesterol ratio. Improvement in blood chemistry was satisfactory in 73 percent, and none of the patients has suffered vascular accidents since beginning the regime. A high pyridoxine intake is stressed as essential to the proper working of lipotropic agents. Patients with angina usually experienced less pain. In 74 percent of patients a satisfactory reduction in blood pressure resulted. The author wonders if the high blood pressure associated with arteriosclerosis might sometimes be other than the "essential" type.

SURE, B.: *Improvement in protein efficiency of a whole wheat cereal breakfast food with the amino acids, lysine and threonine and vitamin B<sub>12</sub>.* Arch. Ped., 69, 9, Sept. 1952, 359-365.

Considerable increase in the protein efficiency of a whole wheat breakfast food was obtained by the addition of 0.4 percent L-lysine monohydrochloride, 0.2 percent DL-threonine in the ration, 0.1 microgram of crystalline vitamin B<sub>12</sub> per animal per day and an extract from condensed fish solubles which introduced 0.196 percent nitrogen in the ration.

SANNEMAN, E. H. AND BEARD, M. F.: *Parenteral B<sub>12</sub>-folic acid therapy in pernicious anemia.* Ann. Int. Med., 37, 4, Oct. 1952, 755-760.

Beard and his co-workers have reported that in certain instances, vitamin B<sub>12</sub> alone is not a complete maintenance therapy in pernicious anemia. Supplementation of B<sub>12</sub> with folic acid was tried in a group of 8 patients whose hemograms had remained subnormal on B<sub>12</sub> alone. Rubrafolin (Squibb) contains 15 micrograms of B<sub>12</sub> and 1.67 mg. of folic acid per c.c. All the patients were given 1 c.c. of this preparation weekly. None of these patients showed any improvement, seven of them showing declines which are probably not statistically significant. At any rate, it was shown that the addition of parenteral folic acid in the dosage used resulted in no significant change in the hematological status.

MITCHELL, H. H.: *Overnutrition and obesity.* J. Clin. Nutrition, 1, 1, Sept.-Oct. 1952, 66-76.

Mitchell feels that it is well to include in the food supply, amounts of essential nutrients in excess of day-to-day requirements. The disadvantages of protein overnutrition have, in the past, been greatly exaggerated and probably do not exist in human nutrition. The problem of obesity is by no means a simple one. The tendency to obesity is probably an inherited, gene-controlled propensity so that the consumption of enormous amounts of fat is not always necessary to produce the condition. The fact that marked obesity is frequently associated with diabetes, hypertension, gall bladder disease and arteriosclerosis does not logically prove a causal relationship. It may even suggest that obesity and these other conditions have a cause in common. Nevertheless, excessive obesity, when present, should be treated by a low fat diet.

SOBEL, A. E. AND ROSENBERG, A. A.: *Physiological availability of vitamin B from capsules.* Am. J. Dis. Child., 84, 5, Nov. 1952, 609-615.

It was found that wide divergence can exist in the physiological availability of vitamin A when administered in the form of multiple vitamin capsules. Three typical multiple vitamin capsules of the same composition were tested. When compared with the maximum

rise for a reference substance (percomorph liver oil) taken as 100 percent, the maximum rise in the blood vitamin A was 198 percent for capsule A, 128 percent for capsule B and only 70 percent for capsule C. In pure aqueous media, both at pH<sub>2</sub> and at pH<sub>7.8</sub>, the capsule with the lowest physiological availability disintegrated first, while the capsule with the highest physiological availability did not disintegrate for several hours.

FISCHER, C. C.: *Nutritional problems in adolescence*. Am. Pract. & Dig. Treat., 3, 12, Dec. 1952, 968-972.

The adolescent is usually neglected from the medical standpoint, but there are "spurts" in the rate of growth, usually between the ages of 12 and 14 which are as great as in the infant, and it is here that sufficient protein, iron, calcium and vitamin D are particularly needed. The treatment of adolescent obesity is similar to that of adulthood. The danger of pulmonary T. B. requires scout films of the chest. The B. M. R. is a poor gauge of the adolescent's metabolism, and much fluctuation may be permitted without undue concern. The author does not mention the obvious over-growth in height and weight of many young people, although it should perhaps be a matter of concern in adolescence.

## EDITORIAL

### STRESS

Hans Selye, whose work on the effects of stress on the animal organism is now known throughout the world, is now bringing out an annual volume dealing with the various reports appearing on this subject. In this work he is assisted by Alexander Horava. The readers of this Journal are no doubt aware that we regard Selye's work as of great significance to medicine, and quite fundamental to physiological research. This

monumental work on Stress is so important that we would like to suggest to all authors, whose subjects bear on this theme, to send reprints as soon as possible to Dr. Selye at the University of Montreal, Montreal, Canada. Such action will give very wide publicity to the reprints, and will also facilitate the continuing efforts of Dr. Selye and his associates to bring before the medical and scientific world all the facts connected with the reaction of the organism to stress.

## BOOK REVIEW

FOOD FOR LIFE. The University of Chicago Press, 5750 Ellis Ave., Chicago 37, Ill. 1952. \$4.75.

Under the authorship of six very distinguished nutritionists, *Food For Life*, which obviously means "Foods which you ought to eat to be well" is written in a semi-popular style, with pen-and-ink drawings which are often humorous, and directs the reader's attention to basic questions in nutrition, covers dietetics, physiology, energy metabolism, and then tackles the difficult problem of future improvement in human nutrition. While the book is presumably meant for popular consumption at the university level, there are passages so technical that possibly only 2 or 3 percent of practicing physicians could grasp their significance. On the whole, however, *Food for Life* is decidedly interesting reading for the physician. The final chapter may perhaps be the finest in the book. Here it is admitted that primitive races, as well as animals, naturally eat those foods which contain the most valuable nu-

trients, as well as minerals. This innate wisdom is the key to survival, and yet it is a *racial* wisdom gained through timeless trial-and-error experience. The authors then pointedly explain that the malnutrition of the present day is often due to sophistication, another name for processed foods. Failure of the soil is a second cause and a third is the necessity for importation of foods from great distances. Ignorance and poverty are two of the personal factors which must be combatted by the physician. The over-use of refined sugar is a weakness of our civilization. From a global standpoint, considering the rapidly increasing population of the world, entirely new methods of food production will almost certainly have to come into use. Producing yeast on wood hydrolysates is one possibility. Restraint of population growth is the obvious solution. At the present moment, education of the average American in nutritional problems is very essential, and we believe the present volume serves that purpose extremely well.

## GENERAL ABSTRACTS OF CURRENT LITERATURE

HARMAN, J. B.: *Esophagitis*. Brit. Med. J., May 3, 1952, 941-945.

Harman, in a masterly way, definitely persuades the reader that our knowledge of esophagitis is most indefinite. The symptoms of esophagitis are pain in the lower chest and heartburn. Dysphagia may be severe, the pain lasting about half an hour. Heartburn, in esophagitis, is characteristically made worse by stooping, which causes reflux of gastric juice into the esophagus. Rosacea is very common in women suffering from esophagitis. The symptoms of esophagitis may be secondary to peptic ulcer of the stomach or duodenum, to cholecystitis, or cancer. The first event in the production of esophagitis is the repeated bathing of the lower end of the esophagus with gastric juice. Congenital short esophagus and hiatus hernia frequently are involved. A chronic, deep ulcer may form. The final outcome of esophagitis is fibrous stricture. In severe cases of esophagitis, surgical treatment is necessary. In medical treatment, alkalis and sleeping upright to prevent regurgitation are of value. What is needed is more frequent use of the esophagoscope to teach us more about esophagitis.

WERELIUS, A.: *Bowel obstruction: a brief resume of its therapeutic evolution*. Illinois Med. J., 101, 5, May 1952, 248-252.

The author reviews the different methods which have historically and currently been employed in treating bowel obstruction. The first great advance was decompression by enterostomy or colostomy as a prelude to the radical operation. This evolved into suction decompression,—one of the most important contributions to intestinal surgery, because it preserves peristalsis by preventing overdistention. Further contributions have been the restoration of fluid and electrolyte balance, the use of antibiotics and last, but not least, scientific anesthesia.

KNOWLES, H. C., FELSON, B., SHAPIRO, N. AND SCHIFF, L.: *Emergency diagnosis of upper digestive tract bleeding by roentgen examination without palpation ("Hampton technic")*. Radiology, 58, 4, April 1952, 536-541.

The source of bleeding in the upper digestive tract must be determined rapidly if we are to make use of the improved medical and surgical technics in management. The authors have shown that the x-ray examination without palpation (Hampton technic) is safe and valuable. In a series of 80 unselected cases examined by this method during a one-year period, a diagnostic accuracy of 86 percent was attained. The Hampton procedure is not advocated to replace regular gastrointestinal x-ray examination, which should always be performed at a suitable interval after bleeding has ceased. Two ounces of a barium mixture are fed and distributed over the gastric mucosa by turning the patient on his right side, then on his back. A double-contrast effect in the bulb may be obtained by rotating

the patient partially onto his left side, and spot films made.

KALLET, H. I. AND DAVLIN, L. P.: *Anal irritation following the use of antibiotics*. Am. Pract. & Dig. Treat., 3, 5, May 1952, 377-378.

Following an influenza epidemic in Detroit in 1950-51, there were many cases using aureomycin and similar antibiotics who, after one or two months, developed severe anal irritation. The chief symptom was itching and burning around the anus. The cause may be an alteration in the bacterial flora of the intestine, or a reduction in B complex absorption. The cases seen by the author were successfully treated by spraying the perianal skin with a 2 percent solution of Pontocaine, after which tincture of benzoin was applied and allowed to dry. Lassar's paste was then spread thinly over the area. This was done twice weekly till complete relief was obtained.

OGILVIE, SIR HENEAGE: *The surgery of peptic ulceration*. Brit. Med. J., Aug. 9, 1952, 299-304.

"All the best people have peptic ulcers." In Britain it is thought that 10 percent of all adults have peptic ulcer. Acid causes ulcers to persist but it does not cause ulcer. In those cases which resist medical treatment, Ogilvie uses gastrectomy, Billroth I for gastric ulcer and Billroth II for duodenal ulcer. The present death rate of 2.7 percent can be reduced to zero. Out of 115 patients operated on recently by the author, only one death occurred, in a man of 66 from extensive mesenteric thrombosis.

OGILVIE, A. G., CARDOE, N. AND BENTLEY, F. H.: *Treatment of massive bleeding from peptic ulcer*. Brit. Med. J., Aug. 9, 1952, 304-309.

Medical treatment consists of blood transfusions, fluid intake, frequent feeding of bland foods and the judicious use of morphine. The decision to operate usually was made where signs of bleeding persisted for 24 hours. Of 358 patients, 10 percent came to operation. The overall mortality was 5.3 percent.

EISENMENGER, W. J.: *Role of sodium in the formation and control of ascites in patients with cirrhosis*. Ann. Int. Med., 37, 2, August 1952, 261-272.

The author presents physiologic mechanisms involved in the production of ascites in advanced Laennec's cirrhosis. The control of ascites by sodium restriction seems to be due to a decreased production of antidiuretic hormone. The low salt diet is usually well tolerated in these cases. By its use, one can avoid the constant waste of plasma protein resulting from numerous paracenteses. The metabolic improvement so obtained may mean the difference between recovery and death.

SANFORD, C. H.: *Primary malignant disease of the liver*. Ann. Int. Med., 37, 2, Aug. 1952, 304-312.

Sanford studied the records of 38 cases of primary malignant disease of the liver occurring in the John

Gaston Hospital from 1920 through 1951. His idea was to find means by which clinical diagnosis could be made prior to death. Laparotomy is by far the best method of confirming such a diagnosis. Resection of a tumor mass, where possible, may be expected to prolong the patient's life. An enlarged, hard, painful, tender, irregular or nodular liver with or without ascites and with or without jaundice, should always make one think of primary malignancy. If present in a male 40 years or more of age, the possibility is greater. If a diagnosis of pre-existing cirrhosis can be established, one can be almost certain of primary cancer of the liver.

GRUNOW, O. H.: *Telepaque and Priodax, gall-bladder media: a comparative study.* Texas State J. M., 48, 8, August 1952, 596-600.

In a series of 128 patients receiving Telepaque as a gallbladder medium, there was a 50 percent reduction in such side effects as nausea, vomiting, diarrhea, dysuria, headache and pyrosis. Telepaque produced no consistent urinary disturbance. It produced consistently more brilliant gallbladder images on cholecystograms than Priodax. The presence of unabsorbed drug in the colon was disturbing but did not interfere with the diagnostic value. A decrease from 3 to 2 grams is warranted and produces only minor changes in the number of symptoms and the brilliance of the image.

GOIN, L. S.: *Some obscure factors in the production of unusual small bowel patterns.* Radiology, 59, 2, August 1952, 177-184.

The author was able to obtain abnormal small bowel patterns in patients by adding the suspected allergen, —usually milk—to the barium suspension, and contrasting the films with those previously made using allergen-free barium sulfate suspension in saline. Segmentation and increased motility with loss of mucosal pattern were the chief findings. Furthermore, delayed emptying of the stomach was sometimes a second finding in such cases. Many of these cases had suffered for years from such symptoms as abdominal pain or nausea and vomiting or constant diarrhea and all of them were cured of their symptoms by omission of the offending substance. In one case "conscience" was the cause of an abnormal small bowel pattern; this occurred in a Jewess when she consciously ate pork, which is interdicted by her religion, but no such pattern resulted when she was given pork without her knowledge, finely comminuted in the barium mixture.

BENNETT, H. S. AND ROSEMILLER, H. R.: *Gastric carcinoma associated with gastroenterostomy.* Cleveland Clin. Quart., 19, 3, July 1952, 116-120.

Three cases are presented in which cancer of the stomach was found, at varying intervals, following gastroenterostomy, presumably for benign gastric ulcer. These cases graphically demonstrate the danger of any operation short of gastric resection for gastric ulcer. All gastric ulcers should be subjected to biopsy and pathological examination.

ROMAN, P. W., WAGNER, J. H., AND STEINBACH, S. H.: *Massive fatal embolism during barium enema study.* Radiology, 59, 2, Aug. 1952, 190-192.

While giving a barium enema to an old lady suffering from suspected obstruction, when the rectum had

been filled, the radiologist noted a peculiar appearance. The patient strained down as if to defecate while the barium assumed a stringy appearance, and it was suddenly realized that it conformed to the shape of the pelvic vessels adjacent to the rectum. A barium embolism via the inferior vena cava produced death in a few minutes. Post mortem examination revealed some barium in the blood vessels of the lungs and kidneys. The point of exit from the rectum was not found and it was assumed that this must have been a small fissure or varix. The passage of barium through the colonic mucosa is a medical curiosity. Only one other case has been reported, in a patient with ulcerative colitis.

PALMER, EDDY D.: *Observations on the vigorous diagnostic approach to severe upper gastrointestinal hemorrhage.* Ann. Int. Med., 36, 6 June 1952, 1484-1491.

Palmer carried out major diagnostic procedures, —esophagoscopy, gastroscopy and x-ray examination —within a few hours after admission to hospital in 121 patients with sudden severe upper gastrointestinal hemorrhage. A positive diagnosis was established in 94 patients. Later, repeated studies permitted a diagnosis on only 10 more. The early use of these diagnostic measures was not detrimental to any of the patients. Blood transfusions may be given during these various examinations. There seemed to be no contraindication to the use of pressure during fluoroscopy. As a result of early diagnosis, early surgical attack was carried out on 19 specific bleeding lesions. Duodenal ulcer, gastric ulcer, hypertrophic gastritis and erosive gastritis were, in order, the most common causes of hemorrhage.

MC EWEN, K. L. AND LODMELL, E. A.: *Acute fulminating idiopathic ulcerative colitis.* Radiology, 59, 2, August 1952, 185-189.

An interesting case of *bona fide* acute thrombo-ulcerative colitis in a young soldier is presented. The ulcerative lesions which were apparent radiographically in the colon completely disappeared within 3 weeks, representing remarkable reversibility. Whether this striking change was due to the aureomycin which was used is impossible to state. He also received many blood transfusions. The case is interesting also because the disease appeared following a court martial for violation of duty regulations. A follow-up two months later showed the disease to be still absent.

GOTTLIEB, C., BERANBAUM, S. L. AND WEINER, M. L.: *Syphilis of the stomach.* Radiology, 59, 2, August 1952, 193-197.

Two cases of gastric syphilis showing antral filling defects are presented. One was proved at autopsy, the other by clinical, roentgen and laboratory methods. In the latter case, following intensive anti-luetic treatment (penicillin and bismuth) the lesion gradually disappeared, so that after 7 months the x-ray appearance of the stomach was normal.

CAPURRO, F. G. AND PECANTEL, J. C.: *A new technic in the study of the mucosal pattern in the cardiac area of the stomach.* Radiology, 59, 2, August 1952, 198-200.

Since the cardiac area of the stomach is not amenable to compression, the authors suggest collapsing the air

bubble as a useful procedure for diagnosis of incipient lesions in this region. This is accomplished (1) by evacuation of the air through a duodenal tube, through which barium can be introduced after aspiration is complete, (2) by pneumoperitoneum or (3) by a combination of the two procedures. Aspiration is best for mucosal relief studies. Pneumoperitoneum is useful for the diagnosis of lesions growing out of the stomach and for differentiation of extragastric lesions.

DOWNIE, V. J.: *Massive hemorrhage from acute gastric ulcer.* Brit. Med. J., July 5, 1952, 24-25.

The chief point of interest in this paper is the demonstration of the fact that the use of large amounts of transfused blood (about 9 to 12 pints) in elderly patients has apparently interfered with the healing of surgical wounds. The author does not theorize upon the possible reasons why this should be so. He has decided to operate on such cases as soon as possible and before too much blood has been given as transfusions. Stored blood was used in the cases described.

SODEMAN, W. A., CHAUDHURI, R. N. and BANERJEE, D.: *Terramycin in active diarrheal and dysenteric amebiasis.* Ann. Int. Med., 36, 6, June 1952, 1467-1474.

In a group of 16 patients with diarrheal and dysenteric amebiasis, terramycin was an efficient drug and successfully replaced emetine in treatment. One symptomatic failure was controlled by emetine. Toxic manifestations occurred in 5 patients but did not necessitate cessation of therapy. The patients were invariably better by the second day. By the 10th day, ulcers were healed. It is not certain that terramycin completely eradicated the parasite and further study is needed. However, there is no doubt that terramycin has a definite place in the treatment of diarrheal and dysenteric amebiasis.

NAKAYA, R., SAKAGUCHI, G. and FUKUMI, H.: *S. Newbrunswick from a food poisoning outbreak and from a healthy carrier.* Japanese J. Med. Sci. and Biol., 5, 2, April 1952, 125-128.

*S. Newbrunswick* was isolated from the stools of patients in a food poisoning outbreak and, at the same time, *S. Senftenberg* was isolated from its presumable causative food. Possibly the latter microorganism became the former, after passage through the human bodies. This is the first report on the isolation of *S. Newbrunswick* either from a food poisoning case or from a healthy carrier in Japan.

LEMON, H. M.: *The application of cytologic diagnosis to cancers of the stomach, pancreas and biliary system.* Ann. Int. Med., 37, 3, Sept. 1952, 525-533.

The cytologic examination of gastric washings and of duodenal drainage fluid, has a definite place in the diagnosis of malignant lesions of the stomach, the pancreas and the biliary system. Special training is required, particularly in the microscopic recognition of cancer cells. The examination of duodenal drainage fluids is somewhat more satisfactory than that of gastric washings, because fewer cells usually are found. An over-all accuracy of 79.5 percent was found for

the methods used by Lemon's group. The method is most valuable where other methods are of no value, and it should eventually result in the early detection of cancer in cases in which it is now detected with difficulty, or too late, or not at all.

WAUGH, T. R. and CHARENDORFF, M. D.: *Gastric cancer on ulcer: a clinical analysis of a series of cases conforming pathologically to the criteria for malignant change in peptic ulcer of the stomach.* Ann. Int. Med., 37, 3, Sept. 1952, 534-542.

Over a 20 year period, at the Royal Victoria Hospital, Montreal, 263 gastric resections were done in which pathological examination showed the presence of cancer. Of these cases, only 10 were found to conform to the rigid criteria necessary to state that a cancer had formed in a peptic ulcer. In these cases the cancer invades the submucosa in the side wall of the ulcer but does not involve the base. The cancer is therefore a "cancer in situ." Some of these cancers metastasized. Sixty percent of the cases are alive and well, as compared with approximately twenty percent five-year cures on all cases having gastric resection for cancer.

CAMPBELL, K. N., SELDEN, L. V. and HAMBURGER, S. W.: *Duodenal diverticulitis treated by diverticulectomy.* Alex. Blain Hosp. Bull., 11, 3, Aug. 1952, 56-68.

A case of symptomatic duodenal diverticulitis is described, which was cured by surgical removal of the diverticulum, the latter showing definite inflammatory changes microscopically. In 1950, two similar cases were reported from the Alexander Blain Hospital. The pain in the upper right abdomen was constant and radiated to the back, and was aggravated by lying down after meals. Occasionally a mass appeared in the epigastrium after meals but always disappeared quickly and spontaneously. The diagnosis was made by x-ray.

MACHELLA, T. E., DWORKEN, H. J. and BIEL, F. J.: *Observations on the splenic flexure syndrome.* Ann. Int. Med., 37, 3, Sept. 1952, 543-552.

Forty patients are presented in whom coronary disease could have been suspected because of characteristic anginal pain distribution but in whom the sole cause of the pain was distention of the splenic flexure of the colon with gas or with feces. Obviously it is important to differentiate between such suspected coronary disease and the "splenic flexure syndrome."

CAMERON, D. G., BENSLEY, E. H. and WOOD, P.: *Latent steatorrhea.* Ann. Int. Med., 37, 3, Sept. 1952, 553-558.

Tetany, osteomalacia, megalocytic anemia and iron deficiency were the presenting symptoms in 8 cases which were finally diagnosed as latent steatorrhea, the latter requiring fat balance studies for diagnosis. Folic acid, liver extract, intravenous saccharated iron oxide, calcium lactate and vitamin D by mouth, vitamin K, and also multiple vitamin preparations, constituted the effective treatment. No dietary restrictions were imposed.

### NATIONAL HEART INSTITUTE

Fifteen young physicians have recently been given special training awards under the clinical traineeship program of the National Heart Institute, Surgeon General Leonard A. Scheele, Public Health Service, Federal Security Agency has announced. A total of 32 physicians are now receiving heart traineeships, studying in 25 institutions in 12 states and the District of Columbia.

Since the inception of the program 4 years ago, 149 physicians have been given the opportunity to acquire special skills in diagnosing and treating the heart diseases which afflict about nine million people in the United States. The majority of these doctors have completed their periods of study and are helping to relieve the serious shortage of physicians who understand techniques of interpreting electrocardiograms, carrying out cardiac fluoroscopy and correlating various diagnostic findings. These doctors will apply and develop their new skills to improve the health or lengthen the lives of the people they treat, whether as staff members of cardiology departments in hospitals, or in carrying on a high level of private practice.

Traineeships carry stipends of \$3,000 per year for trainees without dependents and \$3,600 for those with dependents. Eligible for such special study are doctors who are citizens, who have completed a general internship, have at least one additional year of experience or training, and are not over forty years of age. Applications for the traineeships may be obtained from the National Heart Institute, Public Health Service, Bethesda 14, Maryland.

### DR. HARVEY M. MERKER ELECTED PRESIDENT OF DETROIT LIBRARY COMMISSION

Detroit, Jan. 7.—Dr. Harvey M. Merker has been elected president of the Detroit Library Commission for a one-year term, the Commission announced today.

The Commission is responsible for administration of the Detroit Library and its 26 branches throughout the city. Commissioners

are appointed by the Detroit School Board to six-year terms, and its president is elected by the Commission.

Dr. Merker, Director of Inventory Control and Consultant on Chemical and Pharmaceutical Manufacturing at Parke, Davis & Company, succeeds Thomas Long, attorney, as Library Commission President.

The Detroit Library Commission recently has received national attention for its program of making community centers out of branch libraries, with meeting rooms and study groups for neighborhood organizations, and for their high degree of administrative efficiency in the handling and lending of books.

The Detroit library system annually distributes more than five million books. It is especially noted for its extensive history of the automobile industry and for its Burton collection on the Great Lakes region and the Northwest Territory. The library was organized in 1865, and one of its early users was Thomas A. Edison, who studied at the Detroit Library during his off-hours as a newspaper boy on a railroad.

Dr. Merker, a native Detroiter, holds 16 separate offices in civic, church and philanthropic organizations in the area. He also has made more than 500 lectures on medical and scientific papers and is co-author of the pharmaceutical manufacture section in the *Encyclopedia of Chemical Technology*.

At present, Dr. Merker is president of the Detroit Institute of Cancer Research, director of the Better Business Bureau, chairman of the National Advisory Council of the Michigan Memorial Phoenix Project, an elder of the Fort Street Presbyterian Church, governor of the University of Michigan Club of Detroit, and governor of the Rackham Research Foundation, Michigan State College. He is a trustee or member of a host of other organizations.

Last June, Dr. Merker observed his 45th anniversary with Parke-Davis, where his first job was moving 100-gallon drums of glycerine. In 1919, he became assistant superintendent of the manufacturing division and a year later was named to head manufacturing operations at the Parke-Davis Walkerville (Ont.) plant.

In 1922, he returned to Detroit and seven years later became superintendent of the manufacturing division. He assumed his present position early this year.

Dr. Merker was born three blocks from the present Parke-Davis headquarters site and was graduated with honors from Central High School. He received a B.S. degree in chemical engineering from the University of Michigan and in 1940 was awarded the honorary degree of Master of Engineering from that institution. In 1943, he received the honorary degree of Doctor of Science in Chemistry from Wayne University.

### MEETING IN RICHMOND

Richmond, Va., Dec. 9.—Each of the nation's Governors has an invitation before him today to name a 75-year-old doctor to attend the first western hemisphere conference of the World Medical Association as a guest of honor. It will be held at Richmond, Va., April 23 to 25, 1953.

The invitations were extended by John S. Battle, Governor of the host state, to the 47 other Governors, asking that a senior physician from each state come to Virginia and bear witness to medical advances that have taken place within his lifetime.

The 75-year-old guests, who carried medicines to their first patients in saddlebags or by horse and buggy, will travel to Virginia by Pullman or plane. They will be greeted by Dr. Louis H. Bauer, president of the American Medical Association, and by medical leaders of Latin America. Included in the program will be visits to the state's historic spots and opportunities to recall the discovery of x-ray, vitamins, blood transfusions, powerful new drugs and other advances that have lengthened human life.

"I am sure your nominee will have a pleasant and rewarding visit and be accorded the recognition due a distinguished representative of the medical profession," Governor Battle wrote. He will appoint the guest physician for Virginia.

Travel and other expenses of delegates from the medical societies of the American republics and of the 75-year-old guests—for a pro-

gram of the doctors' own choosing—are being met through a grant by E. Claiborne Robins, whose grandfather founded A. H. Robins Co., Inc., ethical pharmaceutical house of Richmond, 75 years ago.

"During the lifetime of physicians now 75, the average length of human life in our country has nearly doubled," Governor Battle observed, "and Mr. Robins believes that recognition and honor are due those who have witnessed these advances and had a part in them."

Dr. Bauer, announcing the World Medical Association meeting recently, said that three quarters of a century ago, life expectancy at birth was 34 years among industrial policyholders of a large life insurance company and a few years more for the population at large. Today's life expectancy, he said, is 68—alike for the industrial and general population. It is expected to pass 70 well before 1960 if present medical gains continue. The conference will survey what lies on the horizon, not only for the United States but for all the Americas.

Besides reviewing these medical gains, the 75-year-old physicians will tour Virginia's springtime gardens and historic sites, including the 18th century Williamsburg restoration and St. John's Church in Richmond, where Patrick Henry declared, "Give me liberty or give me death."

#### AMERICAN CAN COMPANY HOLDS LARGEST SALES SEMINAR IN HISTORY

The largest sales seminar in the history of American Can Company is being held in New York for salesmen from the company's 34 district sales offices in the U. S. and Canada. T. E. Alwyn, vice president in charge of sales reported.

The seminar, which got under way on January 12, 1953 at Canco's headquarters, is in the form of a series of meetings extending over six months. Only 25 salesmen will attend each session so that a more thorough and closer study can be made of every subject on the agenda.

A feature of the seminar will be the use of case studies involving actual sales problems, Mr. Alwyn said, rather than the conventional lecture type of instruction used at sales meetings. Each case to be dis-

cussed is a carefully disguised description of an actual can company sales situation. The salesman will be given the opportunity to analyze the case, interpret the problem, and arrive at a solution based on group judgment.

The case studies, moderated by Kenneth R. Andrews, associate professor of business administration at Harvard University, are designed to cultivate broader reasoning by full evaluation of all the complex factors involved in sales problems.

#### HAZARDOUS, INFECTIOUS DISEASES STUDIED AT CLOSE RANGE IN NEW VIRUS RESEARCH LABORATORY AT PARKE, DAVIS & CO.

Highly hazardous and infectious diseases are being studied at close range here in a new virus research laboratory just completed at Parke, Davis & Company.

"The specially-designed new building—one of the few of its kind in the world—allows more critical studies of every type of virus investigation," Dr. Leon A. Sweet, vice-president and director of research for the 86-year-old firm, has disclosed.

Under the supervision of Dr. F. D. Stimpert, director of microbiological research, Parke-Davis scientists are conducting important experiments involving polio, "Q" fever, the common cold, mumps, measles and other highly infectious diseases which are difficult in ordinary laboratories.

The scientists, headed by Dr. I. W. McLean and Dr. A. R. Taylor, who direct virus research, will be equipped to seek new data about even such unusual and hazardous diseases as Japanese "B" encephalitis (inflammation of the brain), equine encephalomyelitis (combined inflammation of the brain and the spinal cord) and Russian Spring and Summer Diseases (a tick-borne brain fever).

#### No Chance for Diseases to Be Carried Outside Lab

The new virus laboratory is a one-story brick and steel structure, 100 feet long and 40 feet wide.

A penthouse contains machinery for three air-conditioning and three heating systems.

Moderately in size because of the nature of the work, the building

constitutes a compact, self-contained unit made up of five working rooms which can be sealed off and decontaminated quickly and easily. A special enamel finish on the walls allows steam or disinfectant sterilization and decontamination.

Isolation units for several thousand animals, ranging from mice to monkeys, hold cross-infection to a minimum. In one room, each monkey has an individually-regulated and air-conditioned cage. In the ordinary laboratory, scientists are frequently handicapped by the involuntary infection of some animals by others.

Each unit is self-contained, with no reason for cages, food or equipment to be taken outside. Attendants change their clothing, take showers and use disinfectant before leaving the building.

Dr. Stimpert declared, "There's no chance for any of the diseases to be carried beyond the laboratory."

Even the waste and air are sterilized, he said.

#### Scientists Work Under Special Ultra-Violet Hoods

There are special ultra-violet hoods under which the Parke-Davis scientists work on eggs and cultures.

Air is exhausted with high-pressure steam.

Dr. Stimpert said major projects include the study of chemotherapeutic agents for infectious diseases; new vaccines for the immunization of humans; and fundamental research on the nature of various viruses.

A virus is a living micro-organism which can grow only in a living cell, he explained.

"With the aid of the most modern of electron microscopes, research studies now in progress promise further improvements in influenza vaccine and other antigens," Dr. Stimpert said. "Many new types of virus are under investigation. Virus purification is being more completely elucidated."

The electron microscope enables the scientists to magnify an object 1,000 to 22,000 times directly and up to 150,000 times photographically. The ordinary microscope magnifies only 10 to 1,300 times.

The new virus research laboratory is among the more than 50 buildings which constitute the Parke-Davis home offices and laboratories here on 27 acres along the

north bank of the Detroit River, facing Windsor, Ontario.

The pharmaceutical firm, which makes more than 1,000 different medicinals, has plants, branches or depots in 30 United States and Canadian cities. In addition, it has nine overseas branches and plants, others under construction and many direct distributor relationships elsewhere abroad.

#### THE PHYSICIAN'S BULLETIN

In step with the busy schedule of today's doctor, Eli Lilly and Company has conceived an entirely new format for its house publication *The Physician's Bulletin*. Starting in January, 1953, the new "PB" is designed to give brief, concise information in a handy form to the 150,000 doctors who receive it.

The publication changes from its former 8½ x 11 size to a new 5 x 7¾ "pocket-book" size. Also, it has been increased from twenty-four to thirty-two pages. Brevity will be the keynote in the copy, and full-color illustrations will be used throughout. Formerly published six times a year, the new "PB" will be issued ten times a year, appearing every month except August and December.

*The Physician's Bulletin* is edited by S. O. Waife, M.D., with the assistance of other physicians who serve full-time on the Lilly staff.

#### PRICE REDUCTION

Eli Lilly and Company, which discovered and developed the new wide-range antibiotic "Ilotycin" (Erythromycin, Lilly), has announced, effective January 5, 1953, a 26-percent reduction in its price. At the same time, Lilly's reduced prices on certain items in its penicillin, streptomycin, and dihydrostreptomycin line.

Commenting on the "Ilotycin" price reduction, J. K. Lilly, president of the company, said: "We have every reason to hope that "Ilotycin" will repeat the price history of most new drugs. The initial price reflects the cost of extensive research and development and also a company's limited experience in producing the new item. Under our American process of competition, any manufacturer must look sharply at his price just as soon as he develops better yields and more efficient means of production."

APRIL, 1953

#### MEPHATE

Mephate in capsule form is announced by the A. H. Robins Co., Inc., Richmond, Va., as a means of heightening the clinical usefulness of orally administered mephenesin by the inclusion of glutamic acid hydrochloride to improve absorption and enhance effectiveness. Upon absorption, mephenesin acts within the central nervous system to diminish the irritability of certain areas or nerve elements in the spinal cord, brain stem and cerebral cortex.

Each capsule contains 0.25 Gm. mephenesin and 0.30 Gm. glutamic acid hydrochloride. Mephate is indicated in such diverse clinical conditions as anxiety tension and psychotic states; acute and chronic alcoholism; rheumatoid arthritis and other rheumatic conditions; certain neurological and spastic disorders such as Parkinsonism, cerebral palsy, multiple sclerosis, low back pain and disc syndromes; control of tetanus convulsions, and certain forms of epilepsy.

Dosage must be individualized because of the diversity and amenability to treatment of these clinical states but, with adults, should start with two tablets orally three or four times daily, then adjusted as necessary to achieve maximum results.

Though serious side effects are not to be anticipated with Mephate, medication should coincide with the taking of food, fruit juice or other nourishment. As mephenesin and barbiturates act synergistically, their concurrent administration is to be watched carefully.

Mephate is supplied in bottles of 100 and 500 blue and white capsules.

#### HIGHLY-PURIFIED ACTH INTRODUCED BY BREON

A purified form of corticotropin (ACTH) is now being offered to doctors, hospitals and the drug trade by George A. Breon & Co., pharmaceutical manufacturer, under the trade name of El-Acorto Gel. It supplements the firm's previously-introduced ACTH preparation, Acorto Gel.

Chief advantage of the purified product is that it is more easily liquefied at lower temperatures than the regular ACTH in the depot preparation. Breon notes that

El-Acorto Gel contains virtually no foreign material and, consequently, will remain "flowable" at approximately room temperature.

The company observes a growing trend towards the use of ACTH preparations. Clinical tests show that ACTH does not produce irreversible changes in the body, and that it stimulates the production of all adrenocorticoids, it is stated.

El-Acorto Gel is indicated in treatment of rheumatoid arthritis, acute rheumatic fever, ulcerative colitis unresponsive to the usual therapies, and many allergic manifestations, including severe bronchial asthma. Usual dose is 40 to 60 units given either subcutaneously or intramuscularly, once or twice daily. It is supplied by Breon in 5 c. c. multidose vials in two potencies. Each c. c. contains purified ACTH equivalent in clinical activity to either 40 or 80 U. S. P. units of corticotropin.

#### TANTER ELECTED VICE-PRESIDENT OF N. Y. ACADEMY OF SCIENCES

Election of Dr. David B. Steinman and Dr. Maurice L. Tainter as president and vice-president of the New York Academy of Sciences was announced following the Academy's 135th annual meeting held recently.

Dr. Tainter is director of the Sterling-Winthrop Research Institute and a vice-president of Sterling Drug Inc., of which the Institute is a division. A former Professor of Pharmacology at Stanford University and of Physiology at Albany Medical College, Dr. Tainter has been associated with Sterling since 1943.

He is a fellow of the American Association for the Advancement of Science, and a member of the American Chemical Society, American Pharmaceutical Association, American Medical Association, Society of Medical Jurisprudence, and other professional and scientific organizations. He has been a consultant on chemical warfare defense to the civilian defense organizations since 1942, and is on the editorial board of "Archives Internationales de Pharmacodynamie et de Therapie."

Other officers elected for the 1953 term by the N. Y. Academy

of Sciences, fourth oldest scientific society in the country, included: Dr. Paul Fejos, president-elect; Dr. Elmore H. Northey, vice-president; Mr. Junius Bird, corresponding secretary; Mr. John Tee-Van, recording secretary, and Mr. Donald M. Benjamin, treasurer.

### NICE WORK

Members of the Linen Supply Association of America, located in virtually every town and city of importance in the United States, will display large colorful posters on each side of their delivery vehicles during the entire month of March advocating the sound advice of "Good Health Is Precious—Have a Check-up Regularly."

This continuing campaign is a contribution of the Linen Supply Industry in the belief it is of public service.

### PRECISION EQUIPMENT CO. ISSUES NEW CATALOG

Precision Equipment Co. has just published a new catalog featuring Steel Shelving, Lockers as well as other storage and maintenance equipment for industrial and institutional use. This new catalog continues to feature, in the tradition of previous Precision catalogs, the work of nationally famous cartoonists. The new catalog also contains the popular joke column entitled, "Heard in the Locker Room," which adds additional sparkle to Precision catalogs. Write Precision Equipment Co., 3712 N. Milwaukee Ave., Chicago 41, Illinois for your copy.

### NEW TECHNICAL PAPERS FEATURED IN PHOTOGRAPHIC SCIENCE AND TECHNIQUE

The February, 1953, issue of "Photographic Science and Technique," the quarterly journal produced by the Technical Division of the Photographic Society of America, contained ten new technical papers of more than general interest to advanced workers.

One of the most important of these is Part II of "The Present Status of Direct and Negative-Positive Color Print Processes in Europe" by Dr. Heinz Gordon of the Swedish Colorphoto Corporation.

This paper discusses positive print materials and processing including means of identifying the various types of films, the use of light balancing and mosaic filters, additive printing, the sensitivity characteristics of Agfacolor, Gavacolor, Ferriacolor, and Telcolor papers and exposure and processing of color papers.

Other articles of interest are as follows:

*Two-Bath Fixation of Prints by J. J. Crabtree, R. W. Henn, and R. F. Edgerton of the Kodak Research Laboratories.* This paper discusses the factors involved when two successive fixing baths are used instead of one. The technical advantages of two fixing baths over one are discussed and the economy of two-bath fixation is pointed out—it being possible to process 200 prints per gallon as against 50 in a single bath with the same final degree of print permanence.

*Photographic Standards for Camera Shutters by Vernon E. Whitman of Graflex, Inc.* This paper discusses four new American standards providing for uniformity of calibration and performance characteristics of focal plane and between-the-lens camera shutters which have just been approved by the American Standards Association. The paper details the history of the shutter project, basic considerations in scope, defines the terms employed, and provides some information on application of the standards. New American standards in the field of motion pictures covering raw stock cores for 16mm motion picture film and edge numbering of 15mm motion picture film, are also discussed briefly.

*Submarine Periscope Photography by J. C. Milligan of the Kollmorgen Optical Corporation.* This paper describes the space in which a photographer must work when he is using a periscope as a camera, the problems of record and reconnaissance photography, available cameras, exposure determination, focusing procedures, the use of ray filters, and the processing and printing of film aboard a submarine.

*A communication by G. L. P. Levenson on behalf of the Scientific and Technical Group of the Royal Photographic Society of Great Britain.* This communication dis-

cusses the mechanism of photographic sensitivity in silver bromide. It notes that it has been recently shown by Loening that pure silver bromide in the form of an aqueous salt has only a very slight sensitivity to light as judged after development. Sensitization can be achieved by adding various substances. These substances probably react with the silver bromide to form minute quantities of silver, gold, and silver sulfide respectively at the grain surfaces.

*"Modification of Lacquers for Protective Coating of Photographs," by Hubert O. Rangea of the Plastic Coating Corporation.* This paper discusses a number of promising new components which have recently been examined with a view toward supplementing or replacing present lacquer constituents in the treatment of photographic prints.

*"Motion Picture and Flash Photography in Mechanics Research" by Clifford C. Hauver of the Navy Department, Naval Reserve Laboratory.* This paper deals principally with examples of the events and equipment used for pictures of very fast operations taken at very high speeds.

*Some Design Features of a Wide-Film Continuous Processing Machine by J. S. Goldhamer of the Department of the Air Force, Wright Air Development Center.* This paper describes equipment designed for processing aerial film and prints therefrom at a rate of approximately 20 feet per minute in normal D-1 developer at 85°F without supplementary hardening. A number of the problems involved in designing such equipment and making it practical for field use are described.

*The Influence of Quaternary Salts on Photographic Development and Their Effectiveness as Chromatographic Developers* is discussed in communication No. 1519 from the Kodak Research Laboratories by W. Vanselow and T. H. James.

*High Speed Photography in Medicine by John H. Waddell of the Wollensak Optical Company.* This paper discusses high-speed motion picture applications to the study of various organs and the techniques and results obtained from high-speed photographs of the larynx, eardrum, heart, and muscular motion.

## E. W. ZELLER

Appointment of E. W. Zeller as general sales manager of the A. H. Robins Co., Inc., ethical pharmaceutical house of Richmond, Va., has been announced by E. Claiborne Robins, company president. Mr. Zeller succeeds to the position held by the late E. F. Heffner, Jr.

The new sales manager came to the Robins Co. as southern division manager in 1945, with headquarters in Atlanta. In 1951 he transferred to the Richmond Headquarters to become assistant sales manager, while retaining the southern division management.

Mr. Zeller was born in Philadelphia in 1896 and is a graduate of the Central High School of that city and of the University of Pennsylvania, where he became a member of Pi Delta Epsilon. He saw service with the Army Medical Corps in France and Germany in World War I. Since that time he has been in the ethical drug field.

Mr. Zeller, known as Dick to his associates, is married and lives in Richmond.

## E. F. HEFFNER

E. F. Heffner, Jr., vice president and general sales manager of the A. H. Robins Co., Richmond, Va., died suddenly on December 27 at Richmond. He had been in charge of sales for the Robins Co. since 1942. During this 10-year period, the sales organization under his direction grew from some half a dozen men into a large group detailing throughout the United States and Canada.

Mr. Heffner became a vice president of the Robins Co. in 1951. His election to this post was "in keeping with our policy of recognizing outstanding work," according to an announcement made at that time by E. Claiborne Robins, company president.

A native of Lock Haven, Pa., and a graduate of the Philadelphia College of Pharmacy, Mr. Heffner was widely experienced in the pharmaceutical field.

Mr. Heffner is survived by his widow, of 7102 Glen Parkway, Richmond, and by three sons. The eldest, William C. Heffner, is an Episcopal minister. E. F. Heffner, III, resides in Danville, Va., and James J. Heffner in Alexandria, Va.

APRIL, 1953

U. S. VITAMIN MARKETS  
FIRST AQUEOUS VITAMIN-  
MINERAL CAPSULEVi-Aquamin Combines 2 Pioneer  
Triumphs

U. S. Vitamin Corporation and its affiliate, Casimir Funk Laboratories, Inc., announce the availability to the medical, pharmaceutical and allied professions of Vi-Aquamin, the first and only water-soluble multiple vitamin-mineral formula in a single capsule.

Vi-Aquamin combines two pioneering achievements of the U. S. Vitamin Laboratories: (1) development of water-soluble preparations of the normally oil-soluble vitamins A, D and E for more rapid, more complete and more assured absorption and utilization, (2) combining vitamins with minerals based on the studies of Dr. Casimir Funk that vitamins and minerals are nutritionally interrelated.

Vi-Aquamin capsules provide liberal potencies of all the vitamins and minerals known to be essential to human nutrition in convenient oral form, with absorption and utilization which approach that of parenteral therapy. Ingredients include: vitamin B<sub>12</sub> and other B complex factors—water-solubilized vitamins A, D and E—with calcium, phosphorus, iron, cobalt and other trace minerals.

A special method of processing eliminates fish liver oil; there is no fish taste or odor, nausea, regurgitation and sensitivity. Vi-Aquamin is moderately priced for economy that patients will appreciate. Detailed literature on Vi-Aquamin from U. S. Vitamin Corporation, 250 East 43rd Street, New York 17, N. Y.

## DIAMOND ANNIVERSARY

The A. H. Robins Co., Inc., Richmond, Va., wound up a busy year with sectional sales meetings in four cities during the fortnight preceding the holidays. The incoming year, 1953, marks the company's Diamond Anniversary.

Meetings were held in New York, December 8-11; Cincinnati, December 11-13; Denver, December 15-17, and New Orleans, December 18-20. Among those leading discussions were Dr. Eugene L. Jackson, vice president and medical director; E. W. Zeller, assistant sales manager; Dr. Robert S.

Murphy, pharmacologist, and the late E. F. Heffner, Jr., vice president in charge of sales.

E. Claiborne Robins, president, after attending sessions at New York and Cincinnati, returned for a year-end meeting of the Richmond Chamber of Commerce, of which he was president during 1952.

Dedication of the company's new plant, which will consolidate administrative, research, manufacturing, packaging and shipping operations under one roof in a growing industrial area of Richmond, will coincide with 75th anniversary observances in April. In honor of the medical profession, on the occasion of this anniversary, the Robins Co. has made a grant to the World Medical Association, covering the expenses of its first western hemisphere conference. This event will be held in Richmond, April 23-25, 1953.

EVIDENCE THAT FEMALES,  
AS WELL AS MALES, CAN  
HAVE HEMOPHILIA PRE-  
SENTED AT WAYNE U.S.  
BLOOD SYMPOSIUM

Evidence that females, as well as males, can have hemophilia—in which the victim bleeds abnormally from the slightest wound—was presented recently at the Second Annual Symposium on Blood sponsored by Wayne University College of Medicine.

Hemophilia has been considered traditionally as a hereditary disease occurring only in males, but transmitted by females.

Approximately 300 medical people attending the significant sessions heard four Dallas scientists, Drs. J. M. Hill, Gwendolyn Crass, John Ellis and K. P. Wittstruck, all of the Wadley Research Institute and Blood Center, conclude:

"The female hemophilic may be regarded in a new light. The severe clinical hemophilic female probably still results from coincidence of the inheritance of a severe defect from both father and mother. However, lesser degrees of a bleeding tendency in females seem to be possible from inheritance of a defect that in males, at least, is part of the hemophilia picture. Why should such cases not be considered as mild or partial hemophiliacs?"

The same idea was advanced by scientists at the University of North

Carolina, where a dog colony is maintained for the study of inheritance and blood coagulation mechanisms in hemophilia. Dr. Robert D. Langsdell reported, "The canine disease appears to be similar to human hemophilia, both in clotting defect and its inheritance."

The possible existence of another deficiency, whose characteristics are similar to those of hemophilia but which is definitely distinct from that disease, was reported by Drs. Sidney G. White and Paul M. Aggeler, both of the University of California.

Dr. Elwood A. Sharp, director of clinical investigation for Parke, Davis & Company, presided at the morning session in which other papers on hemophilia also were presented by scientists from Wayne University and Jefferson Medical College of Philadelphia.

*Two Reports Are First of Their Kind Ever Made*

Throughout the day at the internationally-important symposium, the medical people heard top-ranking scientists from several states discuss latest advances in the study of blood. Twenty-five different papers were read.

Those who presided at the sessions, besides Dr. Sharp, were Dr. Walter H. Seegers, Wayne physiology professor and general chairman of the symposium; and Dr. Wolf W. Zuelzer of Children's Hospital, Detroit. The scientists were welcomed by Dr. Gordon H. Scott, dean of the Wayne University College of Medicine.

In the first such report ever made, two Massachusetts Institute of Technology scientists—Drs. David Waugh and Francois Lamy—described the molecular weight and other physical and chemical characteristics of prothrombin, a substance present in plasma and essential for the clotting of blood. This study was difficult because prothrombin is a protein usually destroyed by laboratory manipulations.

In another original report, also the first of its kind, Dr. Seegers and Dr. Norma Alkjærsg, both of Wayne, told of comparing properties of prothrombin as obtained from human and bovine plasma.

Three scientists from the Atomic Energy Commission at the Uni-

versity of Michigan—Drs. H. Petrenco, J. Penner and F. H. Bethell—presented a paper on problems related to irradiation injuries.

Other papers dealing with various other blood subjects were read by scientists from Henry Ford Hospital, Mayo Clinic, University of Leeds, Ohio State University, Mercy Hospital, Baltimore, and the University of Southern California.

Dr. Seegers said the scientists were brought together at the symposium for the purpose of "cross-fertilization of ideas from one specialty to another."

Parke, Davis & Company was host to the scientists at a buffet luncheon and mixer.

**pHISOHEX USED TO  
CLEANSE OPEN WOUNDS  
IN FROSTBITE**

Use of the detergent pHisoHex to cleanse dirty wounds in frostbite cases is recommended as part of a course of immediate treatment designed to reduce the spread of infection in the tissues, according to a report published in GP (7:34, January 1953), by Dr. Gerald H. Pratt, associate professor of clinical surgery, New York University.

Emphasizing the danger of severe cold to civilians as well as soldiers, he describes frostbite symptoms and outlines prophylactic measures and principles of treatment. Immediate treatment of lesions is important, but the type of therapy employed will depend upon the degree of exposure, with many patients requiring only hygienic care.

Early administration of antibiotic drugs to treat open wounds is suggested, as is the use of stimulants in shock cases. Dirty wounds should be cleansed with great care to prevent any tissue injury, Dr. Pratt states, adding that atraumatic cleansing can be accomplished with pHisoHex, the antiseptic detergent widely used in hospitals as a pre-operative scrub.

Treatment in the intermediate stage, the period from the second to the 12th week, is of "utmost importance to the patient," the author notes. The extremities should be kept clean and exposed to air until the wounds heal or separation of the eschar occurs when sterile dressings are applied. To help in

the separation of dead tissue, warm, sterile saline soaks are given one hour each day and the sulfonated detergent pHisoHex is used adjunctively. The use of a whirlpool type bath is also of value.

pHisoHex is supplied by Winthrop-Stearns, Inc.

**BRAND NAME FOR HYDRO-CHOLERETIC ANNOUNCED  
BY GEORGE A. BREON**

George A. Breon & Company's brand of sodium dehydrocholate injection has been given the trademark name of Dilabil-Sodium and the firm's dehydrocholic tablets are now being marketed as Dilabil-Tablets, according to a company announcement.

Dilabil-Sodium is a sterile, aqueous solution of sodium dehydrocholate, 20 per cent, for intravenous use. As a hydrocholeretic, the preparation acts to prevent biliary stasis by stimulating drainage of the bile ducts. In addition, it is an adjunctive prophylactic against the formation of stones. In cholecystography, the combination of Dilabil-Sodium with oral administration of an opaque dye speeds X-ray visualization of gallbladder shadows.

The solution is supplied by Breon in 5 cc ampuls, boxes of 25. Dilabil-Tablets, 0.25 gm dehydrocholic acid, are available in bottles of 100.

**VITAL KOREAN WEAPON  
NEVER SEES COMBAT**

One of the most vital of all weapons in the struggle for life in Korea never sees action at the front.

Mention of the micro-porous filter would draw a blank from the combat man; yet many of his buddies might have died without it.

Use of the filter is the key step in the processing of whole blood into life-giving plasma. The Gas Appliance Manufacturers Association, several of whose members produce the wonder device, describes it as a china-like porcelain filter with pores so tiny that they block blood bacteria while allowing the precious liquid itself to seep through.

Before the development of the micro-porous filter, the two major ways of sterilizing a liquid were either to add a germicide or heat to a point where bacteria would be boiled to death.

Production of these highly specialized filters, GAMA says, de-

pends upon heat processing with gas since it is the only fuel that can provide the exact ranges of temperature and the critically controlled atmospheres necessary to their manufacture. The filters go through several gas-fired kilns before they emerge in their final form.

Besides being used in the processing of blood plasma, the filters also are important factors in making wonder drugs, vitamins, insulin, and in cancer research.

Micro-porous filters are so called, logically enough, because the pores through which the liquids pass are measured in microns or fractions of microns. A micron is 1/254,000 of an inch.

#### GAMMA GLOBULIN FOR MEASLES AND HEPATITIS

New York, Mar. 13.—Recently, the National Foundation for Infantile Paralysis completed negotiations for the purchase of the present inventory of certain processors of commercial gamma globulin as well as the future production by these same producers. In agreement with the American National Red Cross all gamma globulin processed from Red Cross donated blood, as well as the commercially produced gamma globulin purchased by the National Foundation, has been placed under control of the Office of Defense Mobilization. The National Foundation does not have in its possession or control any supply of the blood fraction.

It has been agreed by all parties concerned that gamma globulin will be available for measles prophylaxis and for use by physicians in the treatment of infectious hepatitis, irrespective of the resulting limitation of gamma globulin available for use in poliomyelitis epidemics.

The Office of Defense Mobilization will allocate the available gamma globulin through State and Territorial Health Officers for use in measles and infectious hepatitis, and will make additional distribution for the purpose of controlling poliomyelitis.

Physicians who are unable to purchase gamma globulin through their regular drug supply channels are advised to request supplies from their local or state health departments. There will be no charge for this gamma globulin, since the Red Cross has already paid for the proc-

essing and packaging of the material, and the National Foundation for Infantile Paralysis, through its arrangement with the commercial processors, has purchased the commercial supply at the same rate as that currently supplied defense agencies under governmental contract.

The National Foundation does not have gamma globulin available for distribution, nor will it determine how available supplies shall be used. That is the function of the Office of Defense Mobilization.

Since it has been obvious for some year and a half that gamma globulin would be in short supply, the above plan was agreed upon by all interested agencies, governmental, private and public, to avoid wasteful use of gamma globulin.

#### FOUR STUDIES REPORT ATABRINE EFFECTIVE IN LUPUS ERYTHEMATOSUS

Results ranging mainly from "good" to "excellent" have been noted in the treatment of chronic discoid lupus erythematosus with the antimalarial drug Atabrine, according to four separate medical reports.

Lupus erythematosus is a rare and baffling disease characterized by skin eruptions on various parts of the body, presumed to be caused by an allergy. Some types of the ailment with systemic involvement are fatal.

Independent studies with Atabrine were conducted by Dr. James Sommerville and associates, Glasgow University, Scotland, (*British Journal of Dermatology*, 64:417, Nov. 1952), by Dr. H. H. Sawicky, et al.; Dr. Jean A. Cramer, et al.; and by Dr. George C. Wells (*Journal of Investigative Dermatology*, Dec. 1952). Atabrine dihydrochloride is supplied by Winthrop-Stearns Inc.

In the Sommerville study, Atabrine produced good to excellent results in 19 of 23 patients, slight improvement in three patients, and no improvement in one case. Included in the series was one case classified as subacute disseminated lupus erythematosus. Dosage in all four studies was usually 0.1 gm., three times daily, until yellow pigmentation became marked, at which time the same dose was administered once a day. Atabrine proved more

effective than previous methods of treatment, including bismuth, gold, Vitamin E, sodium salicylate and nicotinamide, the authors state.

They add that the results achieved suggest Atabrine "is the drug of choice in the treatment of lupus erythematosus."

Summarizing tests at the Skin and Cancer Clinic, New York University Hospital, Dr. Sawicky notes that 21 of 30 patients studied showed "prompt and definite improvement," six of whom were completely cleared of lesions without relapsing. Only three patients failed to respond satisfactorily, or relapsed while on therapy or soon after the end of therapy.

Suggesting further clinical evaluation of Atabrine, the report says:

"If the chronic discoid form and subacute and acute disseminated lupus erythematosus are indeed etiologically the same disease, it may be hoped that Atabrine will prove invaluable and perhaps life-saving in the more acute systemic varieties."

In a third study, favorable responses were obtained promptly in five of six cases without any harmful side effects, the only reaction noted being skin discoloration. According to Drs. Jean A. Cramer and George M. Lewis, the most pronounced improvement coincided with the degree of yellow pigmentation, with maximum staining of the skin noticed in the third and fourth weeks of therapy. All of the more recent lesions cleared within four weeks, and only the atrophic scarring present before administration of Atabrine remained at the end of two months.

Of 12 cases treated by Dr. George C. Wells, nine showed a good response with substantial regression of lesions, and of these, three cleared completely. No response was obtained in three cases. The paper cites "dramatic" improvement when Atabrine was used in one case of severe disseminated lupus erythematosus of the face, neck, arms and legs with slight systemic involvement.

#### DISPENSER FOR LUBRICATING JELLY

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#### ANNUAL CONVENTION OF THE INTERNATIONAL ACADEMY OF PROCTOLOGY

All physicians are cordially invited to attend the Fifth Annual Convention of the International Academy of Proctology to be held at the Plaza Hotel, New York City, May 29, 30 and 31st, 1953, directly preceding the American Medical Association Meeting. The meeting this year will be extended to include a Surgical Clinic and Seminar at Jersey City Medical Center under the direction of Dr. Earl J. Halligan. The "Wet Clinic" and Seminar will be on May 28th. An extensive Motion Picture Seminar of Proctologic Surgery (including office techniques) will be held on May 31st. All scientific papers will present the latest developments in proctology and gastroenterology.

Because general practitioners, as well as gastroenterologists and proctologists, face proctologic problems in their daily practice, much of the program has been planned to answer their questions.

There is no fee for attendance at the Annual Convention of the International Academy of Proctology. These Conventions, as well as all other activities of the Academy, are directed toward the further development of proctology. All physicians interested in proctology are therefore invited and welcomed to the Annual Meeting.

The program will be available in

the near future, upon request to the Executive Offices of the International Academy of Proctology, 43-55 Kissena Blvd., Flushing, New York.

#### BEHAVIOR DISORDERS IN CHILDREN REDUCED BY USE OF ELIXIR BENADRYL

New York.—Children with behavior disorders have shown improvement when treated with Elixir Benadryl, two New York physicians report.

Dr. Abraham S. Effron and Dr. Alfred M. Freedman, both of New York, said (Journal of Pediatrics, 42:261, 1953) that 61 percent of the 44 patients treated with Elixir Benadryl responded favorably.

The two physicians reported Benadryl appears to be most satisfactory in the treatment of primary behavior disorders, especially in those patients who show considerable anxiety.

The major usefulness of Benadryl, the physicians observed, "seems to be its effect in reducing anxiety and, at the same time, improving relationship problems to significant adults."

Drs. Effron and Freedman reported that children with sleep disturbances, especially night terrors, seem to obtain rapid relief from symptoms with a general improvement in behavior.

No toxic symptoms were observed in any of the children due to the administration of the drug, the physicians said.

The dosage schedule of Elixir Benadryl was 10 mg. three times a day for the first week; 20 mg. three times a day for the second week; 30 mg. three times a day for the third week; and during the last week of treatment, 30 mg. four times a day.

Patients were chosen at random—34 male and 10 female children between the ages of 6 and 12 years. Of these, 20 were diagnosed as schizophrenic, 13 were organic, eight were primary behavior disorders, two were psychopathic, and one was mentally defective, the physicians said.

Changes were recorded in seven categories, and of the 61 percent that showed improvement, 49 percent did so in three to five categories and 12 percent in one or two categories.

Drs. Effron and Freedman noted a reduction in manifest anxiety in 54 percent of the cases; an improvement in the child's relationship with adults was found in 56 percent of the cases; and 44 percent of the children showed improved relationship with other children.

"In those cases in which depression was the prevailing mood, 37 percent benefited by elevation of mood," the physicians observed. "Of those children who were hyperactive during the preliminary observation period, there was a reduction of this hyperactivity in 29 percent with Benadryl."

A broad international program of research in tropical medicine and health problems, including nutrition, will be initiated immediately in Liberia, West Africa, it was announced today by Dr. Edward L. Salisbury, president of the Liberian Institute of the American Foundation for Tropical Medicine.

In his announcement of the broadened research program of the Liberian Institute, Dr. Salisbury revealed that Dr. Max J. Miller, formerly Associate Professor in the Institute of Parasitology of Macdonald College, McGill University, who has been appointed research director of the Liberian Institute, will depart for Harbel, Liberia, to take full charge of the Institute operations and direct research activities centered in that institution.

The Liberian Institute was established in 1946 by the American Foundation for Tropical Medicine for the purpose of stimulating comprehensive and exhaustive research in the causes, treatment, and control of tropical diseases. One hundred acres of land was donated for the Institute by the Liberian Government, and construction of the laboratory, administration, and the first residential buildings was accomplished through a gift of \$250,000 by Harvey S. Firestone, Jr., as a memorial to his father. Since the completion of the buildings in January, 1952, the Institute has been used as a base of operations by a United States Public Health Service mission.

The Liberian Institute's immediate objective, according to Dr. Salisbury, is to launch an investigation into the prevalence and importance of tropical diseases in Li-

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and should not be used indiscriminately or for minor infections —  
and, as with certain other drugs, adequate blood studies should be  
made when the patient requires prolonged or intermittent therapy.

Chloromycetin is a notably effective, well tolerated, broad spectrum antibiotic





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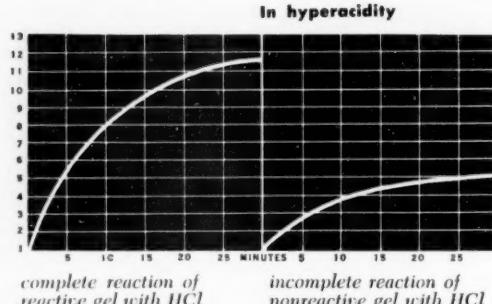
Calories? Virtually none.

1. Smith, F. H.: *Gastroenterology*, 8:494, Apr., 1947.  
2. Woldman, E. E.: *Am. Jour. Med. Sc.*, 194:333, Sept., 1937.  
3. Fox, J. R.: *Jour. Lancet*, 72:361, Aug., 1952.

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beria with the aim of initiating and carrying out a vigorous program for the control and eventual eradication of these diseases. It is also planned that the Institute will provide a specialized laboratory center in which medical, governmental, educational, and industrial scientists can unite in a common drive to conquer tropical diseases. Facilities will be made available to visiting scientists and graduate medical students, with restriction to nationality, to carry on independent research in the fields of health and nutrition in the tropics.

The Institute is expected in time to become an international center for research in three basic problems which have retarded development of tropical countries: diseases of man, diseases of domestic animals, and production of balanced food crops for both man and animals. Dr. Salisbury pointed out that improvement of animal husbandry in all tropical countries is essential to any solution of the chronic protein deficiency which contributes to malnutrition and susceptibility to disease of populations in the tropics.

In anticipation of the time when this part of the Liberian Institute's program can be undertaken, the Liberian Government has given the Institute an option on an additional six hundred acres of land for research and experimentation in the feeding, husbandry, and pathology of tropical livestock.

"With the appointment of a Research Director for the Liberian Institute, the American Foundation for Tropical Medicine is beginning an aggressive campaign against tropical diseases," said Dr. Salisbury, "not only in Liberia, but wherever their prevalence serves to shorten human life, to undermine health and efficiency, and to retard social and economic development."

"In this undertaking, the Foundation will ask the support of American business and industry, for business and industry will profit directly from any discoveries that improve health and living standards in tropical countries. Tropical countries are not only rich and largely untouched reservoirs of essential resources, but they constitute the world's last major undeveloped and potential markets. The progress of medical research and health standards in the tropics paves the way for new economies and new

markets; and is, therefore, of sound business value."

An important phase of Liberian Institute activities, according to Dr. Salisbury, will be to make provision for the education of physicians in the highly technical problems involved in treatment and control of tropical diseases. "In this field, it will fill an important need since American students studying for a career in tropical medicine, as doctors or as sanitation officers, are now seriously handicapped by lack of adequate facilities for studying the ecology of tropical diseases, and for field training," he said. "Today graduates seeking opportunities for field work are limited almost entirely to the few large companies operating in the tropics which maintain medical departments."

Dr. Salisbury pointed out that Liberia offers an excellent vantage point for a research center in tropical diseases, since many of its health problems are duplicated in other tropical areas. The country has long been an endemic center for malaria, sleeping sickness, filariasis, elephantiasis, schistosomiasis, and many other parasitic diseases, for yaws and other spirochete diseases, for numerous dysenteries—some of which are not yet classified—and for many virus diseases.

Scientific activities in the Institute will be under the direction and supervision of a Scientific Advisory Committee of the American Foundation for Tropical Medicine, composed of scientists who are faculty members of twenty-four universities, colleges, and representatives of industrial organizations.

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# Searle Research Progress Report:

Continued investigational work has resulted in Pro-Banthine, a new anticholinergic drug with high potency, small dosage, minimal side effects, agreeable taste and convenient dosage schedule.

The new anticholinergic, Pro-Banthine\* (brand of propantheline bromide) provides a powerful drug in the therapy of peptic ulcer, intestinal hypermotility and other conditions of parasympathotonia.

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Pro-Banthine has a pronounced inhibiting action on stimuli at (a) the parasympathetic and sympathetic ganglia and (b) the effector organs of the parasympathetic system.

Pro-Banthine is produced for oral use in 15 mg. sugar-coated tablets.

**SEARLE**  
Research in the Service of Medicine

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*Top*—Section through duodenal bulb just distal to pylorus through center of ulcer crater.

*Center*—Healing ulcer with scar tissue and regeneration of tissue layers.

*Bottom*—Healed ulcer with restoration of mucosa.

